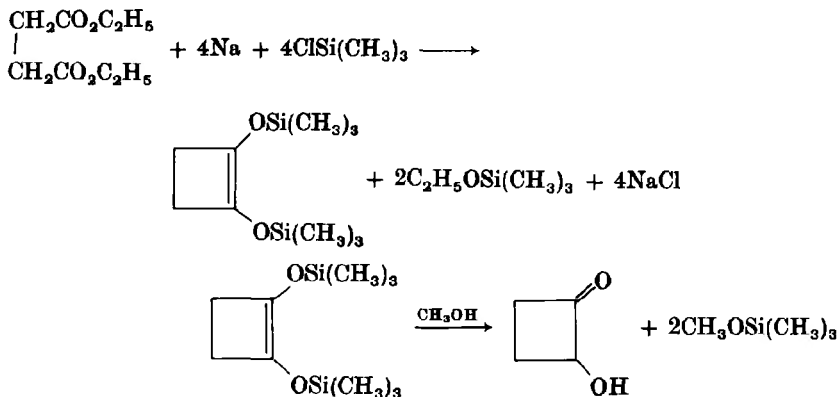


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ACYLOIN CONDENSATION IN WHICH CHLOROTRIMETHYLSILANE IS USED AS A TRAPPING AGENT: 1,2-BIS(TRIMETHYLSILYLOXY)-CYCLOBUTENE AND 2-HYDROXYCYCLOBUTANONE

[Trimethylsilane, 1-cyclobuten-1,2-yleneedioxybis- and Cyclobutanone, 2-hydroxy-]



Submitted by JORDAN J. BLOOMFIELD¹ and JANICE M. NELKE
 Checked by Ž. STOJANAC and Z. VALENTA

1. Procedure

Caution! See warnings concerning the use of impure chlorotrimethylsilane (Note 8) and finely dispersed alkali metals (Notes 1, 9, 11, and 19).

A. 1,2-Bis(trimethylsilyloxy)cyclobutene. *Method 1.* A 1-l., three-necked, creased flask is fitted with a stirrer capable of forming a fine dispersion of molten sodium (Note 1), a reflux condenser, and a Hershberg addition funnel and maintained under an oxygen-free, nitrogen atmosphere. The flask is charged with 250–300 ml. of dry solvent (Note 2) and 9.6–9.8 g. (~0.4 g.-atom) of freshly cut sodium (Notes 3, 4). The solvent is brought to gentle reflux and then the stirrer is operated at full speed until the sodium is fully dispersed (Note 5). The stirrer speed is reduced (Note 6) and a mixture of 17.4 g. (0.1 mole) of diethyl succinate (Note 7) and 45–50 g. (~0.4 mole) of chlorotrimethylsilane (Note 8) in 125 ml. of solvent is added over one to three hours. The reaction is exothermic and a dark purple precipitate appears within a few minutes (Note 9). The solvent is maintained at reflux during and

after the addition (Note 10). After five hours of additional stirring, the contents of the flask are cooled and filtered through a 75-mm. coarse sintered-disk funnel in a nitrogen dry-box (Note 11). The precipitate is washed several times with anhydrous ether or petroleum ether.

The colorless to pale yellow filtrate is transferred to a distilling flask, solvent is evaporated, and the residue is distilled under reduced pressure (Note 12). After a small forerun (0.5–1.0 g.), the product is obtained at 82–86° (10 mm.) as a colorless liquid, 18.0 g. (78%), n_D^{25} 1.4331 (Note 13).

Method 2. In the apparatus described above is placed 4.8–5.0 g. (~ 0.2 g.-atom) of clean sodium and 8.0–8.2 g. (~ 0.2 g.-atom) of clean potassium (Notes 3, 4). The flask is heated with a heat gun to form the low-melting alloy, and then 300–350 ml. of anhydrous ether is added from a freshly opened can. The stirrer is operated at full speed until the alloy is dispersed and then at a slower speed for the remainder of the reaction (Notes 5, 6). A mixture of 17.4 g. (0.1 mole) of diethyl succinate (Note 7), 44 g. (0.4 mole) of chlorotrimethylsilane (Note 8), and 125 ml. of anhydrous ether is then added at a rate sufficient to keep the reaction under control (Note 14). The purple mixture is stirred for another 4–6 hours (Note 9) and then filtered and washed as above in a nitrogen dry-box (Note 11). The product is distilled as above; forerun 0.5–2 g. to 80° (10 mm.) and then at 82–86° (10 mm.) as a colorless liquid, 13.8–16.1 g. (60–70%), n_D^{25} 1.4323–1.4330 (Notes 15–19).

B. 2-Hydroxycyclobutanone. In a 1-l., three-necked flask fitted with a magnetic stirring bar, a sintered-disk gas-inlet tube, a dropping funnel, and a reflux condenser is placed 450 ml. of reagent-grade methanol (Note 20). Dry, oxygen-free nitrogen is vigorously bubbled through the methanol for about 1 hour. Then 23 g. (0.10 mole) of freshly distilled (Note 21) 1,2-bis(trimethylsilyloxy)cyclobutene is transferred under nitrogen to the addition funnel and added dropwise to the stirred methanol. Stirring under a reduced nitrogen flow is continued for 24–30 hours (Note 22). The methanol and methoxytrimethylsilane are removed under reduced pressure, and the residual 2-hydroxycyclobutanone is distilled through a short-path still as a colorless liquid, b.p. 52–57° (0.1 mm.), 6.1–7.4 g. (71–86%), n_D^{25} 1.4613–1.4685 (Notes 23–25).

2. Notes

1. Generally a "Stir-O-Vac" stirrer (available from Labline Instruments, Inc., Melrose Park, Ill.) is used. A Vibromixer type of stirrer is

also satisfactory, especially when high-dilution conditions are required. Either stirrer is used in the submitter's laboratory in conjunction with a short condenser surrounding the stirrer shaft to prevent loss of solvent or reactants. The condenser is required in high-dilution procedures with the Vibromixer to protect the diaphragm from solvent vapor. A plain sleeve stirrer with a Teflon paddle was used by the checkers, but the submitters warn that a Teflon paddle with highly dispersed metal, especially sodium-potassium alloy, is dangerous; explosions have been reported when Teflon and molten sodium are in contact. The submitters also emphasize that, because the large particle size can cause or lead to side reactions, in general a fine dispersion of metal is desirable, even with chlorotrimethylsilane.

2. Toluene is commonly used. It can be dried by molecular sieves or direct distillation from calcium hydride into the reaction flask. Solvent stored over calcium hydride for several days is usually sufficiently dry to decant directly into the reaction flask, but distillation gives more consistent results. Any solvent with a boiling point sufficiently high to melt sodium is satisfactory. The submitters have also used methylcyclohexane and xylene in acyloin condensations. After the sodium is dispersed, the high-boiling solvent can be removed and replaced with anhydrous ether (as noted by the submitters) or can be retained and used in combination with ether (checkers).

3. The submitters routinely used a nitrogen dry-box to clean, cut, and weigh alkali metals. The checkers cut and weighed these metals under dry toluene.

4. An excess of metal is used because aromatic solvents are reduced to some extent and it is easier than weighing out the exact amount.

5. One or two minutes of a "Stir-O-Vac" operated through a variable transformer at full voltage is required.

6. A setting of 30-40 volts on the variable transformer is used.

7. Diethyl succinate was obtained by the submitters from Eastman Organic Chemicals and used without purification. The checkers obtained the ester from British Drug Houses, Ltd., and distilled it at 100° (11 mm.). In general, it is preferable to distill or crystallize and dry all esters before attempting acyloin condensations.

8. The chlorotrimethylsilane, obtained from Eastman Organic Chemicals (submitters) and Aldrich Chemical Co. (checkers), was distilled from calcium hydride under nitrogen and then stored and weighed in a nitrogen dry-box. *Caution! It is particularly important that*

the chlorotrimethylsilane be distilled, preferably from calcium hydride, under nitrogen. In at least one laboratory² the use of this reagent without prior purification has led to explosions. Chlorotrimethylsilane may contain some dichlorodimethylsilane as an impurity. The dihalosilane hydrolyzes more readily than the monochlorosilane. Cautious treatment with a small amount of water, followed by distillation from calcium hydride, under nitrogen, removes this impurity. A further cautionary note concerning these reactions is also necessary. The explosions occurred in reactions run on a scale larger than 0.1 mole, using undistilled chlorotrimethylsilane and following a published procedure.³ This procedure requires mixing all the reagents at 20–30° and then gradually warming the mixture. When this procedure was applied to diethyl pentanedioate on a large scale, the reaction became uncontrollably exothermic at about 50°. It is recommended that the ester and chlorosilane be added together, dropwise, at a rate sufficient to maintain the exothermic reaction. It is often unsafe with many esters, to have a large amount of unreacted ester in the reaction mixture at any time.

9. The purple color seems to be indicative of a satisfactory reduction. When the color is light or no color develops, the yield is usually poor. Sometimes no reaction occurs. In this instance it is best to discard all residues (*pyrophoric*) carefully and start over with scrupulous attention to dryness of all apparatus and reagents.

10. This is the usual procedure. The submitters report that equally good results are obtained if all the dispersing solvent is replaced by ether and the reaction is run at room temperature. The checkers have found a slightly modified procedure in which refluxing toluene (90 ml.) is used for dispersion, anhydrous ether (250 ml.) is added without removal of toluene, additional ether (120 ml.) is used for addition of diethyl succinate and chlorotrimethylsilane, and the mixture is heated under reflux for 14 hours, to be particularly convenient and to give consistently high yields (77–86%). The checkers have also found that prior removal of toluene does not affect the yields but simplifies final purification. With toluene as solvent, better results are usually obtained at or near reflux. The amount of time following completion of addition of the ester is not critical. (It may vary with the compound being reduced.) The submitters generally use 4–6 hours or overnight, whichever happens to be more convenient.

11. Since a slight excess of metal is used, some may be left over. The excess chlorosilane and the product are sensitive to moisture. To

avoid unpleasantness due to the pyrophoric nature of finely divided alkali metal residues or to hydrolysis of product or production of free acid from the excess silane the submitters *always* filtered the reaction mixture in a nitrogen dry-box. The checkers used a simple sintered-glass funnel filtration under a stream of dry nitrogen.

12. The submitters used a 250-mm. vacuum-jacketed Vigreux column fitted with a variable take-off head. Any good column should be as satisfactory.

13. The yield varies from 65 to 86%, n_D^{25} 1.4322–1.4338; b.p. 58–59° (2 mm.); 68–70° (6 mm.); 82–86° (10 mm.); 88–92° (13–14 mm.). In twelve separate runs (in toluene, toluene-ether, or in ether), the checkers did not obtain a yield below 76%.

14. The reaction is exothermic. Two hours is more than enough time. Too vigorous a reaction can be controlled by an acetone–dry ice bath.

15. The yields given are those obtained by the checkers. For this particular reaction the submitters have found the product to be cleaner and the yields higher (78–93%) with NaK reduction. This is not necessarily a general observation inasmuch as other reactions can occur with the alloy.⁴ The checkers found that a modification involving formation of the alloy in hot toluene (10 ml.), removal of most of the toluene by a stream of dry nitrogen, and dispersion of the alloy in ether led to somewhat better yields (81–85%). Because of convenience, safety, and reproducibility of yield, they strongly favor Method 1.

16. The product can be examined for purity by proton magnetic resonance or by gas chromatography. The submitters have used XF-1150 columns successfully. Columns with polar sites will strip silyloxy groups from the bis(silyloxy) compounds and are unsatisfactory.

17. Both Methods 1 and 2 have been successfully applied to a wide range of 1,2-diester⁵ and to a variety of other esters.⁶ The use of a high-dilution cycle permits this procedure to be applied to medium- and large-ring acyloins with good to excellent results.

18. The product is stable if stored in a tightly screw-capped bottle. Prolonged exposure to moist air leads to decomposition. The submitters have stored samples for several years with no change in physical properties.

19. *Caution! Disposal of residues must be made with care. When excess metal, especially sodium-potassium alloy, is used, the residues can be pyrophoric!*

20. The submitters used a freshly opened bottle for each hydrolysis.

21. Use of freshly distilled bis(silyloxy) compound is critical in many cases, especially in this example. The yield and, more particularly, the quality of the product deteriorate with the age of the sample. Traces of acid should be avoided because even as little as one drop of chlorotrimethylsilane added to the reaction mixture produces a different product. The longer the reaction time in the presence of acid, the greater is the number of other products formed.

22. The reaction time can be reduced considerably by gentle reflux. It is advantageous to follow the reaction by gas chromatography (see Note 16) if heating is used, because prolonged reflux can lead to side reactions.

23. The wide range of refractive index is related to the time interval between distillation and measurement. The longer one waits, the higher is the refractive index. This is apparently due to rapid formation of dimer.

24. In the infrared, 2-hydroxycyclobutanone has a carbonyl band at 1780 cm^{-1} in chloroform solution. Kept in nitrogen-filled screw-capped vials in the freezing compartment of a refrigerator, 2-hydroxycyclobutanone slowly but completely solidifies as its dimer. The infrared spectrum of the solid in a KBr disk shows no carbonyl. However, a chloroform solution of the solid does show the characteristic 1780 cm^{-1} band, indicating rapid equilibration with the monomer.

25. Air readily oxidizes 2-hydroxycyclobutanone; quantitative conversion to succinic acid occurs on standing in the open for several days.

3. Discussion

The discovery that chlorotrimethylsilane will react *in situ* with alcoholates and the acyloin enediolates^{3,7} provided the opportunity to prepare a wide range of four-membered acyloins for the first time.⁵ In addition, most acyloin reaction yields are improved and some diesters which were found to give Dieckmann condensation product as a result of the base formed concomitantly with the acyloin can now be reductively cyclized in good yield.⁶ The general reaction conditions given for the cyclization of diethyl succinate have been applied to synthesis of four- to eight-membered rings with very good results.^{3,7} Also, when a high-dilution cycle is used, good to excellent results in cyclization of eight- to fourteen-membered rings can be obtained. (Yields are 8, 72–85%; 9, 68%; 10, 58–69%; 11, 48%; 12, 68%; 13, 84%; 14, 67%.)⁸

Use of the trapping agent is recommended as the most efficient method for running acyloin condensations for many reasons. Among them are: (a) the work-up is very simple: filter and distil; (b) the bis-(silyloxy)olefin is usually easier to store than the free acyloin and is readily purified by redistillation; (c) unwanted base-catalyzed side reactions during reduction are completely avoided; and (d) the bis-(silyloxy)olefin can be easily converted directly into the diketone by treatment with 1 mole of bromine in carbon tetrachloride.^{9,10} Other reactions are described in Rühlmann's review and in *Organic Reactions*.¹¹

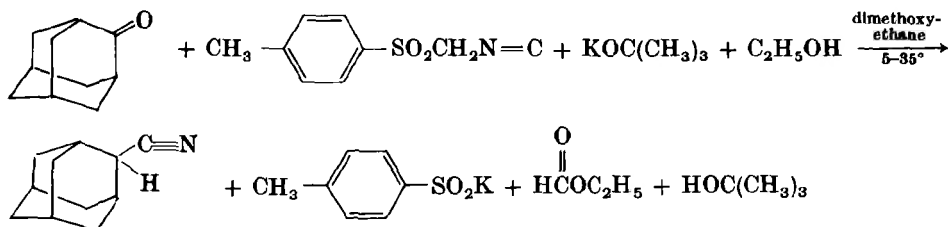
The bis(silyloxy)cyclobutenes are also subject to a variety of special reactions. Probably the most interesting is the observation that they readily undergo a ring-opening reaction leading to a butadiene derivative.⁵ This reaction has already been used to prepare large-ring diketones from cyclic 1,2-diesters.¹²

The synthesis of 2-hydroxycyclobutanone was chosen as a model for the use of a trapping agent because diethyl succinate was the most accessible of 1,2-diesters and because the hydrolysis step for this compound is more difficult than most. Procedures developed for succinoin have been found broadly applicable in preparation of other sensitive acyloins.

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2-ADAMANTANECARBONITRILE

[Tricyclo[3.3.1.1^{3,7}]decan-2-carbonitrile]



Submitted by O. H. OLDENZIEL, J. WILDEMAN,
and A. M. VAN LEUSEN¹

Checked by TERESA Y. L. CHAN and S. MASAMUNE

1. Procedure

A 500-ml., three-necked, round-bottomed flask, equipped with a mechanical stirrer, a thermometer, and a calcium chloride drying tube, is charged with 15.0 g. (0.10 mole) of adamantanone [Tricyclo[3.3.1.1^{3,7}]decan-2-one] (Note 1), 25.4 g. (0.13 mole) of *p*-tolylsulfonylmethyl isocyanide [Benzene, 1-[(isocyanomethyl)sulfonyl]-4-methyl-] (Notes 2, 3), 10 ml. (0.17 mole) of absolute ethanol (Note 4), and 350 ml. of 1,2-dimethoxyethane (Note 5). The stirred solution is cooled in an ice bath to 5°, and 28 g. (0.25 mole) of potassium *tert*-butoxide is added in portions at such a rate that the temperature is kept between 5° and 10° (Notes 6, 7). After the addition is complete, the ice bath is removed and stirring is continued for 30 minutes. Then the reaction mixture is heated for 30 minutes at 35–40°. The stirred suspension is cooled to room temperature and the precipitated potassium *p*-toluenesulfonate is removed by filtration. The precipitate is extracted with three 50-ml. portions of 1,2-dimethoxyethane. The combined 1,2-dimethoxyethane solutions are concentrated to a volume of 25–35 ml. on a rotary evaporator. The concentrated solution is chromatographed (Note 8) through a short column of alumina using distilled petroleum ether (b.p. 40–60°) as the eluent. The combined fractions are refluxed for 15 minutes with 1 g. of activated carbon (Note 9). After removal of the carbon, the solution is concentrated to dryness in a rotary evaporator. The white solid residue is dried overnight in a vacuum desiccator over silica gel to

provide 13.5–14.5 g. (84–90%) of analytically pure 2-adamantanecarbonitrile, m.p. 170–177° (Note 10).

2. Notes

1. Commercial 2-adamantanone (Aldrich Chemical Company, Inc.) was used.

2. The synthesis of *p*-tolylsulfonylmethyl isocyanide is described in this Volume.² The light-brown compound, m.p. 111–114°, was used without further purification.

3. *p*-Tolylsulfonylmethyl isocyanide was used in slight excess in order to effect complete conversion of the adamantanone, which otherwise is difficult to remove from the final product.

4. Commercial absolute ethanol was used.

5. Commercial 1,2-dimethoxyethane, "zur Synthese" quality, was purchased from E. Merck, Darmstadt.

6. Scoops of solid potassium *tert*-butoxide (purchased from E. Merck, Darmstadt, and specified to be at least 95% pure) were added over 20–30 minutes by temporarily removing the drying tube. At the beginning of the reaction much heat is evolved; therefore the base should be added in small portions in order to keep the temperature below 10°. During the addition of the base, a precipitate is formed.

7. The reaction has been carried out successfully with sodium ethoxide also.³

8. The submitters recommend using a 5 cm. by 10 cm. column prepared with 200 g. of neutral alumina (activity I) in petroleum ether (b.p. 40–60°), and eluting with a single 250-ml. fraction of this solvent. The checkers have found that the elution may require more solvent depending on the amount of residual 1,2-dimethoxyethane: they recommend following the chromatography by gas chromatographic analysis (see Note 9).

9. The treatment with activated carbon (purchased from J. T. Baker Chemical Company) can be omitted. In that case, removal of the solvent will provide 14–15 g. (87–93%) of a near-white product with a melting range of 160–180° (see Note 10). Despite this wide range, this material is over 99.8% pure, according to a gas chromatographic analysis carried out at 190° on a 2-m. SE30 column. This high degree of purity was confirmed on three different types of column.

10. Melting points of 2-adamantanecarbonitrile were determined in

sealed tubes to prevent sublimation. Varying values were found for the melting point which apparently is not a very reliable indication of the purity of this compound. A value as high as 184–187° has been found occasionally by following the same procedure. Spectral properties of this product are: infrared (chloroform) cm^{-1} : 2240 (CN); proton magnetic resonance (chloroform-*d*) δ (multiplicity, number of protons): 1.4–2.4 (multiplet, 14), 2.9 (multiplet, 1).

3. Discussion

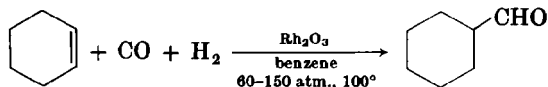
The procedure described is an example of a more general synthetic method for the direct conversion of ketones into cyanides.^{3–6} The reaction has been carried out successfully with acyclic and cyclic aliphatic ketones, including numerous steroidal ketones and aryl-alkyl ketones. The conversion of diaryl or highly hindered ketones such as camphor and β,β -dimethyl- α -tetralone requires the use of a more polar solvent. The dimethoxyethane used in the present procedure should be replaced by dimethyl sulfoxide.⁶

2-Adamantanecarbonitrile was prepared previously by a more laborious method,⁷ also starting from adamantanone in 46% overall yield.

The hydrolysis of 2-adamantanecarbonitrile with hydrogen bromide in acetic acid provides a useful route to 2-adamantanecarboxylic acid (m.p. 143–144°),⁸ which the submitters obtained in 95% yield. Stetter and Tillmans⁷ reported a yield of 62% starting with impure 2-adamantanecarbonitrile.

1. Department of Organic Chemistry, Groningen University, Zernikelaan, Groningen, The Netherlands.
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ALDEHYDES FROM OLEFINS: CYCLOHEXANECARBOXALDEHYDE



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Checked by MARY M. BORECKI, JOSEPH J. MROWCA,
and RICHARD E. BENSON

1. Procedure

To a stainless-steel 0.5-l. pressure vessel (Note 1) equipped with a 450-atm. manometer and a temperature recorder is added 0.2 g. (0.0008 mole) of rhodium(III) oxide (Note 2). The vessel is then sealed and evacuated to 0.1 mm. pressure. A solution of 82 g. (1 mole) of cyclohexene (Note 3) in 140 ml. of anhydrous benzene is introduced by suction into the vessel. The vessel is placed in a heatable shaking device and pressured to 75 atm. with carbon monoxide, then the total pressure is increased to 150 atm. with hydrogen (Note 4). Shaking is begun and the vessel is heated to an internal temperature of 100° (Note 5). When the internal temperature reaches 100°, the pressure begins to fall. Whenever the pressure falls to 60 atm., rocking is stopped and carbon monoxide is first introduced to 105 atm. and then hydrogen to 150 atm. Rocking is started again, and the process is continued until no appreciable pressure decrease occurs. Approximately 2 hours is required, and the pressure decrease corresponds to the consumption of 2 moles of gas. The vessel is rapidly cooled to room temperature (Note 6) and the residual gas is carefully vented.

The vessel is opened, and the slightly yellow reaction mixture is transferred immediately to a 2-l., round-bottomed flask containing a freshly prepared solution of 200 g. of sodium hydrogen sulfite in 400 ml. of water. The flask is fitted with a stopper and is occasionally shaken at room temperature for a period of 3 hours (Note 7). The resulting precipitate is collected by suction filtration on a sintered-glass funnel and washed with 500 ml. of ether (Note 8). After drying in air, the bisulfite derivative is transferred to a 2-l. distillation flask containing 1 l. of 20% aqueous potassium carbonate. The resulting mixture is distilled, and the azeotropic mixture of water and aldehyde (b.p. 94–95°) is collected under nitrogen (Note 9).

The aldehyde is separated from the lower aqueous layer as a colorless liquid and dried over 10 g. of anhydrous sodium sulfate. The drying agent is removed by filtration, and the product is distilled under reduced pressure using a Claisen distillation apparatus to give 92–94 g. (82–84%) of cyclohexanecarboxaldehyde, b.p. 52–53° (18 mm.), n^{25}_D 1.4484 (Notes 10, 11). A purity of about 98% was established by gas chromatographic analysis (Note 12); the product is suitable for synthetic use without further purification (Note 13).

2. Notes

1. The pressure vessel was tested to a pressure of 700 atm. at 300°.
2. The submitters used rhodium(III) oxide available from Fluka A G without further purification. The checkers obtained rhodium(III) oxide from Alfa Inorganics.
3. The cyclohexene was purified by distillation over sodium metal before use (n^{25}_D 1.4452). The submitters used the product available from Fluka A G, and the checkers used the product available from Aldrich Chemical Company, Inc.
4. The purity of the gases used was greater than 99%.
5. During the course of the reaction the temperature was maintained at $100^\circ \pm 2^\circ$.
6. This procedure is useful for avoiding secondary reactions of the aldehydes leading to high-boiling products. It is particularly advisable when linear aliphatic aldehydes are synthesized using cobalt catalysts.³
7. The formation of the bisulfite derivative is an exothermic reaction; the flask is cooled with a bath of cold water for the first 10–15 minutes.
8. It is impossible to obtain a completely white precipitate by this procedure.
9. In order to avoid oxidation of the product the submitters recommend use of a nitrogen atmosphere for all manipulations involving cyclohexanecarboxaldehyde.
10. Literature⁴ values for cyclohexanecarboxaldehyde: b.p. 78.5–80° (57 mm.), n^{25}_D 1.4485.
11. Cyclohexanecarboxaldehyde is stable at room temperature under nitrogen; the submitters noted no appreciable variation in the refractive index after 30 days.
12. The submitters state that gas chromatographic analysis was made on a 2-m. column packed with polypropylene glycol (LB-550-X

available from Perkin-Elmer) on Chromosorb. The retention time at 140° is 5.2 minutes at a flow rate of 30 ml./minute of nitrogen. The 2,4-dinitrophenylhydrazone derivative⁴ melts at 173–174°, and the semicarbazone derivative⁵ melts at 172–173°.

13. In addition to rhodium(III) oxide, cobalt(II) acetylacetonate or dicobalt octacarbonyl has been used by the submitters as catalyst precursors for the hydroformylation of cyclohexene. The results are given in Table I.

TABLE I
HYDROFORMYLATION OF CYCLOHEXENE
WITH COBALT CATALYSTS^a

Catalyst Precursor (mole/l.)	Solvent ^b	Reaction Temperature	Reaction Time (hours)	Yield ^c (%)
[Bis(acetylacetonate) cobalt(II)] (0.08)	Benzene	150° ^d	1.5	70
[Bis(acetylacetonate) ^e cobalt(II)] (0.08)	Heptane	110°	12	74
Dicobalt octacarbonyl ^f (0.006)	Benzene	120°	8	80

^a 4.15 mole/l. of cyclohexene; CO:H₂ = 1:1; 150 atm. initial pressure.

^b 140 ml.

^c The aldehyde was isolated from the reaction mixture through its bisulfite derivative as described in the procedure.

^d Induction time, 40–60 minutes.

^e This catalyst precursor (5 g.) in 140 ml. of heptane was heated in the autoclave at 160° with a mixture of CO:H₂ (1:1) at 150 atm. for 2 hours. The vessel was cooled, the gas released, 1 mole of cyclohexene was charged, and the reaction was carried out according to the usual procedure.

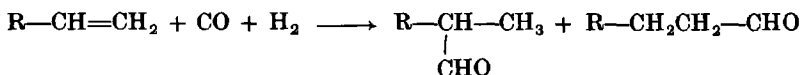
The submitters used product available from Fluka A G that was dried under reduced pressure after recrystallization from heptane at –70°.

3. Discussion

This preparation is an illustration of the hydroformylation of olefins (oxo synthesis). The reaction occurs in the presence of soluble catalytic complexes containing metals of Group VIII of the periodic system. Although the metal originally used by Roelen⁶ and still largely used in the industry for the production of aliphatic aldehydes and alcohols⁷ is cobalt, the most active and selective catalysts are rhodium-containing compounds. The catalytic activity of the other Group VIII metals is in

general much poorer. Although the hydroformylation of unsaturated substrates is a very general reaction,^{7,8} some important limitations associated with the olefin structure may lead to the formation of isomeric aldehydes. In addition, especially in the presence of cobalt catalysts, further reactions of synthesized aldehydes may occur under hydroformylation conditions.

With regard to the structure of the olefins, tetrasubstituted olefins do not undergo hydroformylation reaction under typical reaction conditions, and olefinic substrates containing functional groups sometimes give poor yields and unexpected products.^{7,8} If there is no plane of symmetry in the substrate across the double bond, at least two isomeric aldehydes are obtained.⁹ Although methods for shifting the



isomeric composition of the products have been proposed,¹⁰⁻¹² complete control of the isomeric composition has not been achieved despite the fact that the reaction mechanism is fairly well understood.¹³ In addition, if the structure of the olefin is such that a double-bond shift is possible, isomers other than the two shown above can be formed.¹⁴ Especially when cobalt catalysts are used, further reactions of the synthesized aldehydes may occur, leading to alcohols, aldol condensation products, and acetal derivatives. Some of the secondary reactions can be avoided by carrying out the hydroformylation in the presence of orthoformic acid esters¹⁵ or of other reagents protecting the aldehyde group.¹⁶ However, care must be taken when ortho esters are used, since hydroformylation of ortho esters may occur and yield aldehydes or acetals.¹⁷

Although cobalt catalysts are the best known and the most commonly used, in recent years rhodium has been preferred for laboratory syntheses because of its higher activity and selectivity. As catalyst precursor, Rh_2O_3 ,¹⁸ $\text{Rh}_4(\text{CO})_{12}$,¹⁹ or $\text{HRh}(\text{CO})(\text{PPh}_3)_3$ ¹¹ is commonly used. Rhodium complexes supported on polymers have also been used.¹² For typical organic syntheses the easily accessible Rh_2O_3 seems preferable, even if higher temperature and pressures are required to carry out the olefin hydroformylation. Using $\text{HRh}(\text{CO})(\text{PPh}_3)_3$, olefin hydroformylation at room temperature and pressure is possible.¹¹

The hydroformylation of cyclohexene has been extensively investi-

gated.^{11,12,15,20-22} The present procedure is an adaptation of the rhodium-catalyzed hydroformylation of 2-butene.¹⁸

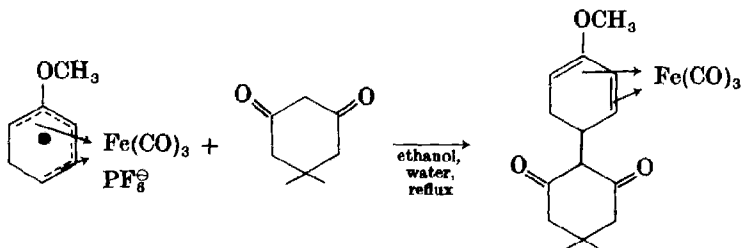
Other methods for the preparation of cyclohexanecarboxaldehyde include the catalytic hydrogenation of 3-cyclohexene-1-carboxaldehyde, available from the Diels-Alder reaction of butadiene and acrolein,²³ the reduction of cyclohexanecarbonyl chloride by lithium tri-*tert*-butoxyaluminum hydride,²⁴ the reduction of *N,N*-dimethylcyclohexanecarboxamide with lithium diethoxyaluminum hydride,²⁵ and the oxidation of the methane-sulfonate of cyclohexylmethanol with dimethyl sulfoxide.²⁶ The hydrolysis, with simultaneous decarboxylation and rearrangement, of glycidic esters derived from cyclohexanone gives cyclohexanecarboxaldehyde.^{4,27}

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**ALKYLATION OF DIMEDONE
 WITH A TRICARBONYL(DIENE)IRON COMPLEX:
 TRICARBONYL[2-[(2,3,4,5- η)-4-METHOXY-2,4-CYCLOHEXADIEN-1-
 YL]-5,5-DIMETHYL-1,3-CYCLOHEXANEDIONE]IRON**

[Iron, tricarbonyl[2-[(2,3,4,5- η)-4-methoxy-2,4-cyclohexadien-1-yl]-
 5,5-dimethyl-1,3-cyclohexanedione]-]



Submitted by A. J. BIRCH and K. B. CHAMBERLAIN¹
 Checked by T. AOKI, S. KAMATA and W. NAGATA

1. Procedure

A 500-ml., round-bottomed flask equipped with a condenser is charged with 5 g. (0.013 mole) of tricarbonyl[(1,2,3,4,5- η)-2-methoxy-2,4-cyclohexadien-1-yl]iron(1+) hexafluorophosphate(1-) (Note 1), 150 ml. of water, and 50 ml. of ethanol and is heated on the steam bath with occasional swirling until the salt is dissolved. Dimedone (1,3-Cyclohexanedione, 5,5-dimethyl-) (2.5 g., 0.018 mole) is dissolved in 50 ml. of ethanol by warming. The two solutions are mixed and refluxed for 15 minutes. After cooling to about 25°, the mixture is poured into 500 ml. of water with stirring and the precipitate is collected, washed with water, and air-dried to yield 4.4 g. of crude product. The product is recrystallized by first dissolving in a minimum volume of boiling ethanol and adding water until the first sign of turbidity. On standing under refrigeration overnight, crystallization occurs. After collection by filtration, the product is washed with water and air-dried to yield 3.7 g. of small white to buff-colored crystals (Note 2), which

darken above 140° but do not melt. On addition of water to the filtrate a further crop of 0.6 g. is obtained. The total yield is 4.3 g. (87%).

2. Notes

1. The preparation of this salt is described in this volume.²
2. Proton magnetic resonance (100 MHz) (acetone-d₆) δ (multiplicity, number of protons): 1.02 (singlet, 6), 1.88 (quartet, 1), 2.23 (singlet), 2.52 (quintet), 2.48–3.52 (multiplet), 3.24–3.52 (multiplet) (preceding four notations account for 10 protons), 3.66 (singlet, 3), 5.24 (quartet, 1); infrared spectrum (Nujol) cm.⁻¹: 2040, 1980, 1950, 1560; mass spectrum m/e : 388 (M⁺).

3. Discussion

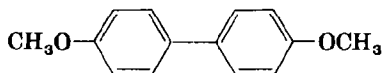
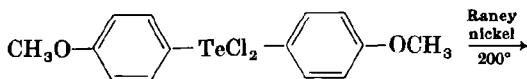
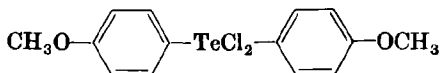
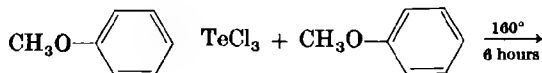
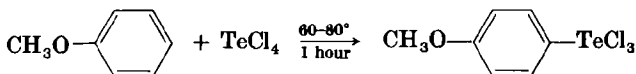
Hexafluorophosphate and tetrafluoroborate dienyl salts react with many nucleophiles.³ The tetrafluoroborate salts are to be preferred, being more soluble in organic solvents than the hexafluorophosphates.

In all cases so far investigated, including a useful direct reaction with ketones,⁴ the methoxydienyl salt is substituted at the 5-position and not at the alternative 1-position. The Fe(CO)₃ group can conveniently be removed from many of these adducts by the action of ferric chloride in ethanol.⁴

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**BIARYLS FROM SIMPLE ARENES *via* ORGANOTELLURIUM
INTERMEDIATES: 4,4'-DIMETHOXY-1,1'-BIPHENYL**

[1,1'-Biphenyl, 4,4'-dimethoxy-]



Submitted by J. BERGMAN, R. CARLSSON,
and B. SjöBERG¹

Checked by J. DIAKUR and S. MASAMUNE

1. Procedure

Caution! Because tellurium compounds have toxic effects similar to those of arsenic compounds,² care should be taken not to bring tellurium tetrachloride and its reaction products into contact with the skin. Avoid breathing fumes and dust of tellurium compounds. In addition, hydrogen chloride is evolved in Step A, and pyrophoric Raney nickel is used in Step B. Therefore all manipulations described in this procedure must be carried out in an efficient fume hood.

A. Bis(4-methoxyphenyl)tellurium Dichloride. In a dry, 500-ml., three-necked, round-bottomed flask equipped with a thermometer and a reflux condenser fitted with a calcium chloride drying tube are placed 27.0 g. (0.1 mole) of tellurium tetrachloride (Note 1) and 64.8 g. (0.6 mole) of dry anisole (Note 2). The mixture is heated to 160° over a period

of 30 minutes and maintained at this temperature for 6 hours. The reaction mixture is allowed to cool to room temperature, and the solvent is removed with the aid of a vacuum pump. The crude solid (Note 3) is dissolved in *ca.* 250 ml. of boiling acetonitrile and filtered while hot (Note 4). Upon cooling to -25° , crystals deposit (Note 5), which weigh 35.5–38.5 g. (84–90%), m.p. $182-183^{\circ}$ (Note 6).

B. 4,4'-*Dimethoxy-1,1'-biphenyl*. A 500-ml., three-necked, round-bottomed flask is equipped with a 500-ml. dropping funnel, a stopper, and a reflux condenser fitted with a two-way stopcock, one end of which is connected to an aspirator, and the other to a cylinder of dry, oxygen-free nitrogen. To this flask are added 60 g. of Raney nickel (Note 7) and 150 ml. of benzene. The system is flushed with nitrogen, and the solvent is evaporated under reduced pressure. The Raney nickel is then degassed behind an explosion shield (Note 8) in a hood by heating to 200° at 2 mm. for 2 hours.

The catalyst is allowed to cool under nitrogen, and 400 ml. of bis-(2-methoxyethyl) ether is added from the dropping funnel. The stopper is then temporarily removed to add 20.6 g. (0.05 mole) of bis(4-methoxyphenyl)tellurium dichloride. The mixture is refluxed for 8 hours, filtered while still hot, and the solvent evaporated under reduced pressure (10–20 mm.). The residue was recrystallized from ethanol to afford 8.5–9.8 g. (78–90%) of the product, m.p. $175-176^{\circ}$ (Note 9).

2. Notes

1. The submitters used tellurium tetrachloride available from E. Merck A G. The checkers purchased the reagent from Research Organic/Inorganic Chemical Corporation.

2. The checkers distilled the anisole from calcium sulfate before use. This reagent functions not only as a reactant, but also as solvent. In some similar preparations the intermediate trichloride is rather insoluble, as in the case of bis(3-methyl-4-methoxyphenyl)tellurium dichloride. The addition of co-solvents such as bis-(2-methoxyethyl) ether is beneficial.³

3. The crude product contains the 4,4'- and the 2,4'-isomers in the ratio 99.2/0.8. See Note 5.

4. A small amount of tellurium (95 mg.) is formed during the preparation. The amount of tellurium increases slowly as the heating is prolonged. In a separate experiment pure bis(4-methoxyphenyl)-

tellurium dichloride was pyrolyzed at 250°. The main products were 1-chloro-4-methoxybenzene and tellurium.

5. Evaporation of the mother liquor gives a solid enriched in the 2,4'-isomer. Recrystallization of this solid from ethanol yields crystals containing 45% of the 2,4'-isomer.

6. The spectral details of the product are: proton magnetic resonance (dimethyl sulfoxide- d_6) δ (multiplicity, number of protons, assignment): 3.80 (singlet, 6, OCH_3), 7.05–8.0 (quartet, 8, A_2B_2 aryl); mass spectrum m/e (relative intensity > 10% for peaks with m/e above 150): 379 (16), 377 (14), 344 (39), 342 (35), 340 (22), 272 (36), 270 (31), 237 (18), 235 (17), 233 (10), 215 (15), 214 (99), 200 (14), 199 (100), 172 (21). No peaks corresponding to the parent ion could be detected.

7. The catalyst was prepared from a nickel–aluminum (50:50) alloy using the procedure given by Mozingo.⁴ The catalyst is used in large excess. Reduced amounts of catalyst resulted in decreased yields, and the product is contaminated with detectable (gas chromatography) amounts of bis(4-methoxyphenyl) telluride.

8. This operation has been performed several times without incident. However, it should be noted that the W6 and W7 forms of Raney nickel have been reported to explode.⁵ No explosions have been reported with the W2 form used in this preparation.

9. 4,4'-Dimethoxybiphenyl can also be prepared by simply refluxing bis(4-methoxyphenyl)tellurium dichloride with degassed commercial Raney nickel. The yields are, however, lower and less reproducible,³ and the product may contain some bis(4-methoxyphenyl) telluride.

3. Discussion

Most synthetic methods for biaryl preparation, such as the Ullmann coupling and all variants of the Grignard coupling,^{6–8} require halogen-substituted aromatic compounds as starting materials. Since these components are prepared by halogenation of the appropriate precursor, either directly or indirectly, it is evident that a direct coupling method offers obvious advantages. Such reactions may be effected electrochemically,⁹ and by reagents such as $\text{Pd}(\text{OAc})_2$,^{10,11} $\text{Ti}(\text{OCOFC}_3)_3$,¹² and VCl_4 .¹³ The applicability of these reagents and the selectivity of the reactions are often restricted, when compared with the present procedure.

Tellurium tetrachloride reacts as an electrophilic reagent with

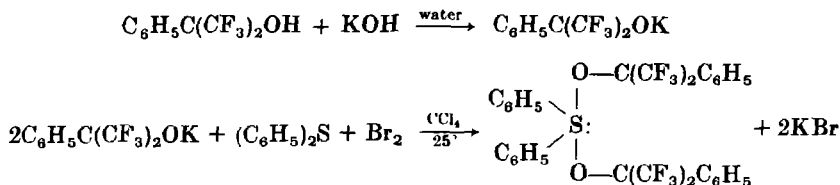
aromatic compounds bearing activating substituents, such as RO-, R₂N- and RS- groups, to provide first aryltellurium trichlorides, and then diaryltellurium dichlorides, as one raises the reaction temperature. The second step should, in order to prevent formation of elemental tellurium and chlorinated aromatics, be performed at as low a temperature as possible (Note 4). This is especially important when highly reactive substrates such as 1,3-dimethoxybenzene are used. The addition of a Lewis acid to the reaction mixture brings about an acceleration of the reaction with less reactive reactants such as benzene and chlorobenzene.³ The rate of acceleration is dramatically enhanced when the ratio of AlCl₃/TeCl₄ is more than 1:1. Thus, refluxing a mixture of 1 equivalent of TeCl₃ and 3 equivalents of AlCl₃ in benzene provided diphenyltellurium dichloride in 58.5% yield.¹⁴

The coupling reaction proceeds better when a rigorously degassed Raney nickel catalyst is used, but a nickel catalyst prepared by a much simplified procedure (Note 9) is also effective. The coupling may also be promoted by other elements, including copper and palladium.

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**BIS[2,2,2-TRIFLUORO-1-PHENYL-1-(TRIFLUOROMETHYL)
ETHOXY] DIPHENYL SULFURANE**

[Sulfur, bis[α,α -bis(trifluoromethyl)benzenemethanolato]diphenyl-]



Submitted by J. C. MARTIN, R. J. ARHART, J. A. FRANZ, E. F. PEROZZI,
and L. J. KAPLAN¹

Checked by H. G. CORKINS, C. J. STARK, and C. R. JOHNSON

1. Procedure

A. *Potassium 1,1,1,3,3,3-Hexafluoro-2-phenyl-2-propanolate* [2-*Propanol*, 1,1,1,3,3,3-hexafluoro-2-phenyl-, potassium salt]. To 25.4 g. (0.39 mole) of 86% potassium hydroxide (Notes 1, 2) dissolved in 50 ml. of water in a 500-ml., round-bottomed flask equipped for simple vacuum distillation is added 100.0 g. (0.410 mole) of 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanol (Note 3). A colorless solution is obtained which is concentrated to a syrup by vacuum distillation using aspirator pressure. Further evacuation with a vacuum pump while heating to 140° results in a white solid. Under the greater vacuum volatile substances can be collected in a trap immersed in an acetone-dry ice bath. The trap must be cleaned or be replaced several times during the first hour. After pumping on the white solid at 140° for 12 hours, the flask is transferred to a glove bag (Note 4) equipped with a mortar and pestle, a vacuum adapter, a powder funnel, a spatula, and a tared 500-ml., round-bottomed flask. Under a dry nitrogen atmosphere the white solid is ground to a fine powder and transferred to the 500-ml. flask. The material is further pumped on (10⁻² mm.) to constant weight. This gives 107–109 g. (97–99%) of potassium 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanolate as a white powder.

B. *Bis[2,2,2-trifluoro-1-phenyl-1-(trifluoromethyl)ethoxy] Diphenyl Sulfurane*. Carbon tetrachloride is distilled directly from phosphorous pentoxide into a dry, 2-l., three-necked flask fitted with stoppers until

700 ml. is collected. The flask is quickly fitted with an adapter for use as a nitrogen inlet, a mechanical stirrer, and an adapter for solid addition (Note 5) to which is attached the 500-ml. flask containing the potassium alkoxide from Part A. A positive pressure of dry nitrogen is used to maintain inert atmosphere conditions. A white slurry is obtained when the powdered alkoxide is added to the stirring carbon tetrachloride at room temperature. Since all of the alkoxide does not transfer, the tared 500-ml. flask is reweighed, and the amount added to the reaction vessel is determined by difference (Note 6). The adaptor used for solid addition is quickly exchanged for a septum.

To a stirring suspension of 105 g. (0.372 mole) of the alkoxide, addition of 34.7 g. (31.0 ml., 0.186 mole) of diphenyl sulfide is made by syringe. Bromine, 29.9 g. (9.6 ml., 0.186 mole), is then added by syringe over a 5-minute period to give a red-brown mixture which gradually fades to a pale yellow during 30 minutes. Stirring is continued at room temperature for 2.5 hours, leaving only a residual pale-yellow color in the solution and a copious precipitate of potassium bromide containing some potassium alkoxide.

A glove bag is equipped with a spatula, a tared 1-l., single-necked round-bottomed flask, a 350-ml. Buchner funnel with filter paper, a 1-l. flask, a vacuum adapter, an aspirator hose (Note 7), and a flask containing 100 ml. of dry carbon tetrachloride. Filtration of the reaction mixture under a nitrogen atmosphere can be achieved by pouring the solution into the filter funnel via one neck of the three-necked flask, which is inserted through a hole in the glove bag. The potassium bromide is removed by filtration and is washed with two 50-ml. portions of dry carbon tetrachloride. The filtrate is then transferred to the 1-l. flask and fitted with the vacuum adapter. After removal of the sulfurane solution from the glove bag (Note 8), the flask is quickly placed on a rotary evaporator (Note 9) and concentrated to a semisolid. Further pumping under reduced pressure (10^{-2} mm.) for 24 hours results in crude sulfurane (115–119 g., 93–96%) as slightly yellow crystals.

The flask containing the crude sulfurane is transferred to the nitrogen atmosphere of the glove bag now containing a powder funnel, a fluted filter paper, a 1-l. single-necked, round-bottomed flask, a 250-ml. graduated cylinder, a 1-l. flask containing 700 ml. of dry pentane (Note 10), and a 500-ml. flask containing 250 ml. of dry diethyl ether (Note 10). After dissolving the sulfurane in 150 ml. of diethyl ether, 500 ml. of pentane is added. A cloudy solution results that clarifies when filtered

directly into the 1-l. flask. The flask is stoppered with the vacuum adapter and removed from the bag. At this time everything but the pentane is removed from the glove bag and the following items are added: a 600-ml. medium-frit sintered-glass funnel, a 1-l., single-necked, round-bottomed flask, a tared 500-ml., single-necked round-bottomed flask, a vacuum adaptor, two spatulas, and a powder funnel. The sulfurane solution is concentrated to *ca.* 350 ml. using a magnetic stirrer to prevent bumping as the solvent is evaporated through the vacuum adapter at reduced pressure and at temperatures not exceeding 40° (Note 9). After a drying tube is connected to the adapter, the flask is cooled in an acetone-dry ice bath to induce crystallization. Swirling the flask during the crystallization prevents crystals from adhering to the sides. When crystallization is complete, the flask is exchanged for the three-necked flask inserted into the side of the glove bag. Cooling in the acetone-dry ice bath is continued while the neck of the flask penetrates the glove bag. The crystals, collected in the sintered-glass funnel by vacuum filtration, are washed with one 50-ml. portion of cold (-78°) pentane and then transferred to the 500-ml. flask. After fitting with the vacuum adapter, the flask is removed from the bag and pumped on (10^{-2} mm.) until the powdered white sulfurane is at constant weight (76–79 g., 61–64%, m.p. 103–108°). Further crystallization from the mother liquors after concentration by rotary evaporation to one-half the original volume gives up to 7 g. of crude sulfurane (m.p. $< 95^{\circ}$) for a total yield of 79–83 g. (63–67%) (Note 11). If analytically pure material is desired, recrystallization by the same method as above gives fine crystals, m.p. 109.5–110.5°.

2. Notes

1. The submitters report no problems in running the entire procedure on four times the scale described here.

2. The use of potassium hydroxide rather than sodium hydroxide is dictated by solubility characteristics which make purification of the sodium alkoxide difficult.

3. The alcohol was obtained from PCR, Incorporated, or was prepared from hexafluoroacetone (E. I. du Pont de Nemours and Company), benzene, and aluminum chloride by the published² procedure.

4. Glove bags can be purchased from Instruments for Research and Industry, 108 Franklin Avenue, Chiltonham, Pa. 19012. The 27 × 27 ×

15 inch bag was found to be a convenient size for this procedure. The submitters performed all inert atmosphere operations in a dry box. All apparatus must be oven or flame dried prior to use.

5. This adaptor consisted of two 24/40 joints connected with Gooch tubing.

6. The quantities of bromine and diphenyl sulfide must be adjusted according to the amount of alkoxide added.

7. A stopcock and a drying tube were inserted into the hose between the glove bag and the aspirator.

8. The other materials in the bag can be removed at this time, but the three-necked flask inserted through the side of the glove bag must not be removed.

9. During solvent removal or recrystallization, temperatures should be kept below 50° to avoid degradation of product quality.

10. Dry ether was obtained by distillation of reagent-grade dry ether from sodium dispersion or by drying over three portions of sodium wire over a 48-hour period. Dry pentane was prepared by adding sodium wire directly to reagent-grade solvent at least twice or by distilling from sodium dispersion.

11. Hexafluoro-2-phenyl-2-propanol may be recovered from mother liquors, recovered solvent, and the KBr salt cake by extracting the mixture with aqueous base. Neutralization of the aqueous phase gives the alcohol (13–23 g.) which is purified by distillation.

3. Discussion

This dialkoxydiphenylsulfurane has been prepared by the reaction of diphenyl sulfide, 2,2,2-trifluoro-1-phenyl-1-(trifluoromethyl)ethyl hypochlorite, and potassium 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanolate³ and by the reaction of diphenyl sulfide with 1 equivalent of chlorine and 2 equivalents of potassium 1,1,1,3,3,3-hexafluoro-2-phenyl-2-propanolate in diethyl ether.⁴

The present method offers several advantages over earlier methods. The use of carbon tetrachloride instead of diethyl ether as solvent avoids the intrusion of certain radical-chain reactions with solvent which are observed with bromine and to a lesser degree with chlorine. In addition, the potassium bromide has a reduced solubility in carbon tetrachloride compared to diethyl ether, thus providing additional driving force for the reaction and ease of purification of product. The selection of bro-

mine instead of chlorine as the oxidizing agent is made in consideration of the ease of handling the bromine by syringe compared to the greater number of operations and more complex apparatus required for chlorine.

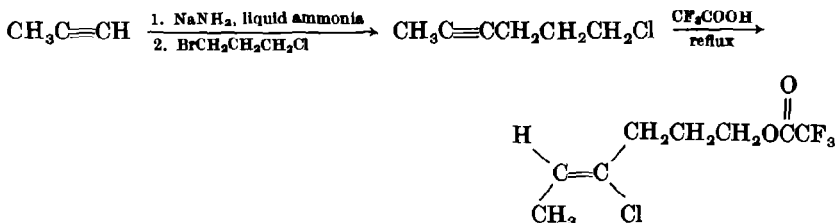
Another dialkoxydiarylsulfurane has been prepared⁵ under conditions similar to those reported here, indicating that this reaction for sulfurane formation may have wide applicability.

The great reactivity of the sulfurane prepared by this procedure toward active hydrogen compounds, coupled with an indefinite shelf life in the absence of moisture, makes this compound a useful reagent for dehydrations,^{6,7} amide cleavage reactions,⁸ epoxide formation,⁹ sulfilimine syntheses,¹⁰ and certain oxidations and coupling reactions.

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(Z)-4-CHLORO-4-HEXENYL TRIFLUOROACETATE

[Acetic acid, trifluoro-, (Z)-4-chloro-4-hexenyl ester]



Submitted by P. E. PETERSON and M. DUNHAM¹

Checked by K.-C. LUK and G. BÜCHI

1. Procedure

A. 6-Chloro-2-hexyne. A 2-l., three-necked, round-bottomed flask is equipped with a low-temperature condenser (Note 1), a gas inlet, and a

magnetic stirrer. Sodium hydroxide drying tubes are placed to precede the inlet and on the condenser. The system is purged with nitrogen, and approximately 650 ml. of anhydrous ammonia (Note 2) is condensed. Freshly cut sodium metal (20.2 g., 0.88 g.-atom) is added to the refluxing ammonia. After dissolution of the sodium (about 20 minutes is required), 0.2 g. of ferric nitrate is added. Two hours of stirring is allowed for conversion of the deep-blue solution of sodium in ammonia to sodium amide. The reaction mixture is cooled to -73° using an acetone-dry ice bath and 50.0 ml. (0.88 mole) of precondensed propyne (Notes 3, 4) is added in portions during a 1-minute period through a glass funnel precooled in dry ice (Note 4). The mixture is stirred with continued cooling for 15 minutes, and 153.5 g. (0.98 mole) of 1-bromo-3-chloropropane (Note 5) is added from an addition funnel during 20 minutes (Note 6). After 30 minutes of additional stirring, 250 ml. of ether is added to the flask and the dry-ice bath is removed. The ammonia is allowed to evaporate (Note 7). Water (200 ml.) is added to the reaction vessel, and the resulting solution is transferred to a 1-l. separatory funnel. The water layer is removed and extracted once with 100 ml. of ether. The combined ether extracts are treated with 6 *M* hydrochloric acid until the aqueous layer is acidic (approximately 20 ml. is required). The ether layer is separated and dried in three stages over magnesium sulfate. Removal of the solvent and distillation of the crude product through a 20-cm. Widmer column (Note 8) gave 49.4–56.0 g. of 6-chloro-2-hexyne, b.p. $58-64^{\circ}$ (20 mm.), which contained some 1-bromo-3-chloropropane (to be removed in the next step). The corrected yield is 29–31% (Note 9).

B. *4-Chloro-4-hexenyl Trifluoroacetate*. A 500-ml., one-necked flask equipped with a magnetic stirrer is charged with 200 ml. of redistilled trifluoroacetic acid (Note 10) and 6-chloro-2-hexyne (0.16 mole, calculated from the gas chromatographic analysis) containing 1-bromo-3-chloropropane. The flask is fitted with a Friedrichs condenser, and the mixture is refluxed for 3 hours; then the flask is transferred to a vacuum distillation apparatus. With the aid of an aspirator and a controlled leak, excess trifluoroacetic acid is removed under slightly reduced pressure, maintaining the pot temperature below 65° to prevent reactions of the acid with the double bond. The remaining trifluoroacetic acid is removed by pouring the product into 100 ml. of ice water and extracting once with 100 ml. and once with 50 ml. of cold dichloromethane. The organic extracts are treated with saturated sodium

hydrogen carbonate (approximately 40 ml.) to pH 7. The resulting aqueous layer is extracted once with an additional 25 ml. of dichloromethane. The combined extracts are dried in three stages by stirring over magnesium sulfate. The final stage is allowed to stand in a refrigerator for 24 hours. The solvent is removed by distillation through a 20-cm. Widmer column (Note 8) at atmospheric pressure. Distillation at reduced pressure gave 16.0–16.4 g. of 4-chloro-4-hexenyl trifluoroacetate, b.p. 86–89° (22 mm.) (Note 11), which contains trace amounts of 1-bromo-3-chloropropane (Note 12). On the basis of the alkyne present in the reactant the yield is 50–52%.

2. Notes

1. A cold finger condenser packed with dry ice and 2-propanol may be used. A Friedrichs condenser in combination with a circulating low-temperature bath (–70°) is more convenient.

2. Ammonia was purchased from Matheson Gas Products.

3. Propyne can be purchased from Linde Specialty Gases or Farhan Research Laboratories. Matheson Gas Products sells propyne also, but only in 100-lb. quantities.

4. The propyne (b.p. –23.2°) is precondensed to the mark in a volumetric flask cooled by acetone-dry ice. Evaporation of some propyne during addition will lead to a moderate molar excess of 1-bromo-3-chloropropane, regarded as desirable in preventing formation of diyne product.

5. 1-Bromo-3-chloropropane was purchased from Aldrich Chemical Company, Inc.

6. Sudden foaming occurred in a run involving insufficient cooling or overly rapid additions. Slow addition could lead to diyne product.

7. The checkers maintained the condenser at –5° during the evaporation to minimize loss of alkyne.

8. The submitters use a platinum spinning band apparatus for the distillation.

9. Gas chromatographic analysis at 79° using a flame detector in conjunction with a 183 × 0.32 cm. stainless-steel column containing Dow-Corning 550 fluid on silanized support gave peaks for 1-bromo-3-chloropropane (6.5 minutes) and 6-chloro-2-hexyne (9.3 minutes) whose areas were shown to be proportional to the mole fractions. The latter were determined by integration of the expanded (50 Hz sweep width)

100 MHz proton magnetic resonance spectrum in the region of overlapping triplets near δ 3.6.

10. The checkers purchased trifluoroacetic acid from Aldrich Chemical Company, Inc., and distilled it from phosphorous pentoxide. The submitters point out that some trifluoroacetic anhydride, whose effects have not been fully investigated, is obtained under these conditions. The submitters prefer to use trifluoroacetic acid which has been distilled through a glass packed column without the use of a drying agent.

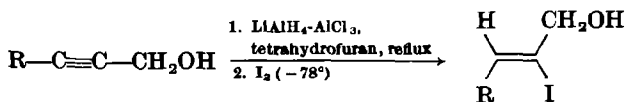
11. n_D^{25} 1.4025; proton magnetic resonance (carbon tetrachloride) δ (multiplicity, coupling constant J in Hz, number of protons): 5.58 (quartet, $J = 7, 1$), 4.35 (triplet, $J = 6, 2$), 2.6–1.8 (multiplet, 4), 1.70 (doublet, $J = 7, 3$).

12. 1-Bromo-3-chloropropane, b.p. 46–55° (15 mm.) is well separated in the early fractions. Gas chromatographic analysis at 120° (cf Note 9) gives peaks of proportional areas for 1-bromo-3-chloropropane (1.2 minutes), 4-chloro-4-hexenyl trifluoroacetate (2.3 minutes), and traces of 4-chloro-4-hexen-1-ol (2.5 minutes).

3. Discussion

The possible presence in the 4-chloro-4-hexenyl trifluoroacetate of small amounts of two *cis-trans* pairs of products of addition of trifluoroacetic to the triple bond without concomitant halogen shift remains speculative. In any event these compounds would be removed as ketones upon hydrolysis² of the trifluoroacetate. Both the 4-chloro-4-hexenyl trifluoroacetate and the alcohol resulting from its hydrolysis have been shown to contain 9% of the (*E*) isomer.² In the present study the hydrogen decoupled ¹³C magnetic resonance spectra of the ester and alcohol were shown to contain peaks attributable to approximately 9% of (*E*) isomer.

Unsymmetrical *trans* vinyl halides have been prepared from acetylenic alcohols by Corey and co-workers³ (as illustrated in the accompanying formulation) in connection with their synthesis of farnesol and *Cecropia* juvenile hormone. Several syntheses of vinyl halides (with

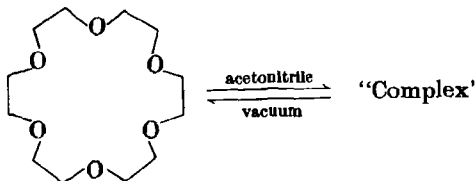
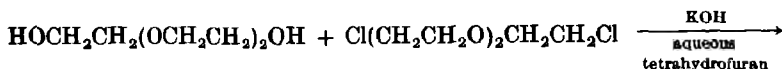


identical R groups, *trans*) have been reported, including procedures involving halogenation and elimination,⁴ addition of hydrochloric acid to alkynes,⁵ and preparation from alkynes *via* vinyl alanes.⁶ The synthesis of unsymmetrical *trans* vinyl halides by 1,4-halogen shift reactions is exemplified by the procedure given here. Such compounds are potentially useful in the synthesis of compounds containing trisubstituted double bonds.⁷

1. Department of Chemistry, University of South Carolina, Columbia, S.C. 29208.
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18-CROWN-6

[1,4,7,10,13,16-Hexaoxacyclooctadecane]



Submitted by GEORGE W. GOKEL,¹ DONALD J. CRAM,² CHARLES L. LIOTTA,
HENRY P. HARRIS,³ and FRED L. COOK³

Checked by E. A. NOE, M. RABAN, and C. R. JOHNSON

1. Procedure

Caution! Crown ethers may be toxic.⁴ Due care should be exercised in the preparation and handling of 18-crown-6. An explosion has been reported

during the thermal decomposition of the crude 18-crown-6-potassium salt complex; see Note 8.

A 3-l., three-necked flask equipped with a mechanical stirrer, a reflux condenser, and an addition funnel is charged with 112.5 g. (102 ml., 0.75 mole) of triethylene glycol [2,2'-(Ethylenedioxy)diethanol] and 600 ml. of tetrahydrofuran (Note 1). Stirring is commenced and a 60% potassium hydroxide solution, prepared by dissolving 109 g. (1.65 moles) of 85% potassium hydroxide in 70 ml. water is added (Note 2). The solution warms slightly. After about 15 minutes of vigorous stirring (the solution begins to develop color and gradually becomes rust brown; Note 3), a solution of 140.3 g. (0.75 mole) of 1,2-bis(2-chloroethoxy)-ethane (Note 4) in 100 ml. of tetrahydrofuran is added in a stream. After the addition is complete, the solution is heated at reflux and stirred vigorously for 18–24 hours. The solution is allowed to cool and the bulk of the tetrahydrofuran is evaporated under reduced pressure (Note 5). The resulting thick brown slurry is diluted with 500 ml. of dichloromethane and filtered through a glass frit. The salts removed by filtration are washed with more dichloromethane to remove absorbed crown and the combined organic solution is dried over anhydrous magnesium sulfate (Note 6), filtered, evaporated to minimum volume (aspirator vacuum) and then distilled under high vacuum using a simple distillation head. The distillation should be carried out at the lowest possible pressure; a typical fraction contains 76–87 g. (38–44%) of crude 18-crown-6 and is collected over 100–167° (0.2 mm.) (Notes 7–9).

To 50 g. of the crude 18-crown-6 in a 250-ml. Erlenmeyer flask is added 100 ml. of acetonitrile. A magnetic stirring bar is added, and the flask is equipped with a calcium chloride drying tube. The resulting slurry is heated on a hot plate to effect solution. The solution is stirred vigorously as it is allowed to cool to ambient temperature; fine white crystals of crown-acetonitrile complex are deposited. The flask is allowed to stand in a freezer for 24–48 hours and is finally cooled in a –30° bath to precipitate as much of the complex as possible. The solid is collected by rapid filtration (Note 10) and is washed once with a small amount of cold acetonitrile. The hygroscopic crystals are transferred to a 200-ml., round-bottomed flask equipped with a magnetic stirring bar and a vacuum takeoff. The acetonitrile is removed from the complex under high vacuum (0.1–0.5 mm.) with gentle heating (~35°) during 2–3 hours. The pure colorless crown (28–33 g., 56–66%) (Note 11) crystallizes on standing, m.p. 38–39.5° (Note 12).

2. Notes

1. The tetrahydrofuran may be used directly without drying or purification.

2. The potassium hydroxide may be added to the water in one portion, but the resulting base solution should be allowed to cool to nearly room temperature before adding to the reaction mixture. If the potassium hydroxide solution is cooled much below ambient temperature, the potassium hydroxide begins to separate; hot potassium hydroxide solution could cause the tetrahydrofuran solution to boil.

3. The rate of darkening is related to the temperature of the solution and, if warm potassium hydroxide solution is used, the color will develop somewhat more rapidly. Differences in the rate of darkening do not appear to affect the yield or purity of product.

4. Available from Eastman Organic Chemicals.

5. As much water as possible should be removed during evaporation so that the salts will filter more readily and the solution can be dried more easily.

6. Drying agents containing complexable cations such as K^+ or Na^+ should be avoided.

7. There is generally a forerun (room temperature to *ca.* 100°) the size of which varies according to the vigor of the previous evaporation steps (see Note 5).

8. In a large batch preparation of 18-crown-6 an explosion has been reported as a result of difficulties occurring during this distillation step.⁵ In this instance the head temperature rose to near 200°. When the system was vented to the atmosphere at this temperature an explosion occurred, apparently the result of autoignition of 1,4-dioxane vapors. Dioxane is reported to undergo autoignition in air at temperatures in excess of 180°. It is recommended that the head and pot be allowed to cool and then be vented with a nitrogen atmosphere.

9. The material obtained in the distillation cut contains both alcoholic and vinylic impurities. The crown may be purified by a second, more careful distillation followed by recrystallization, sublimation or by chromatography in addition to the method described here (see Discussion).

10. The filtration should be conducted in a dry-box or using an inverted funnel-nitrogen flow, whichever is more convenient.

11. The yield of pure crown depends somewhat on the purity of the crude material used. Additional crown may be obtained by combining

mother liquors and repeating the distillation and complex formation process.

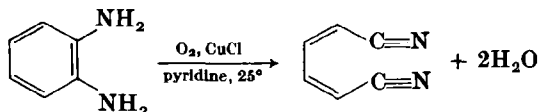
12. The proton magnetic resonance spectrum (carbon tetrachloride) exhibits only a singlet at δ 3.56.

3. Discussion

The compound known as 18-crown-6 is one of the simplest and most useful of the macrocyclic polyethers. Its synthesis in low yield was first reported by Pedersen.⁵ Greene⁶ and Dale and Kristiansen⁷ have reported syntheses of the title compound from triethylene glycol and triethylene glycol di-*p*-toluenesulfonate. Both of these procedures use strong base and anhydrous conditions and achieve purification by more or less classical methods. The combination of distillation and formation of the acetonitrile complex affords crown of high purity without lengthy chromatography or sublimation.^{8,9}

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9. Acknowledgment is made to E. P. Kyba (University of Texas) for noting that this crown can be distilled and to E. R. Wonchoba (Du Pont Co.) for helpful comments.

CUPROUS ION-CATALYZED OXIDATIVE CLEAVAGE OF AROMATIC *o*-DIAMINES BY OXYGEN: [(*Z,Z*)-2,4-HEXADIENEDINITRILE]



Submitted by JIRO TSUJI and HIROSHI TAKAYANAGI¹
Checked by KYO OKADA and WATARU NAGATA

1. Procedure

In a 1-l. three-necked, round-bottomed flask equipped with a mechanical stirrer, a gas-inlet tube, and a dropping funnel is placed 200 ml of pyridine (Note 1). To the flask is added 9.9 g. (0.1 mole) of cuprous chloride (Note 2) which partially dissolves in pyridine to form a yellow suspension (Note 3). Oxygen gas is bubbled into the suspension rapidly for 10 minutes; the suspension changes into a deep-green turbid solution (Note 4). Then 27 g. (0.25 mole) of 1,2-benzenediamine (Note 5) in 300 ml. of pyridine is added slowly from the dropping funnel during 2 hour, while vigorous stirring and bubbling of oxygen are continued (Notes 6, 7). The reaction mixture is transferred to a 1-l., round-bottomed flask, and pyridine is removed under reduced pressure (20 mm.) using a rotary evaporator until a deep-green solid residue is obtained, to which 400 ml. of 6*N* hydrochloric acid and 400 ml. of dichloromethane are added. The mixture is shaken until the solid is dissolved and the lower layer is separated (Note 8). The upper layer is extracted with three 100-ml. portions of dichloromethane. The combined dichloromethane solution is washed with 100 ml. of 5% aqueous sodium hydrogen carbonate, dried over anhydrous sodium sulfate, and evaporated. The brown residue is dissolved in 600 ml. of warm benzene and the solution is filtered through filter paper. When the benzene is evaporated, 23–24 g. (88–93%) of crude product is obtained as a brownish solid. The crude product is recrystallized twice from methanol (7 ml. for 1 g. of the crude material) to yield 19–20 g. (73–77%) of (*Z*, *Z*)-2,4-hexadienedinitrile as colorless needles, m.p. 128–129° (Note 9).

2. Notes

1. Commercial pyridine dried over potassium hydroxide pellets is satisfactory.

2. Reagent-grade cuprous chloride was obtained from Wako Pure Chemical Co., Osaka, Japan.

3. Powdered cuprous chloride should be added in small portions with efficient stirring in order to prevent coagulation.

4. When oxygen gas is bubbled too long, the solution becomes viscous and separation of solid mass occurs, but the mass dissolves with addition of 1,2-benzenediamine.

5. Reagent-grade 1,2-benzenediamine was obtained from Wako Pure Chemical Co., Osaka, Japan.

6. At the moment a drop of the diamine solution hits the reaction mixture, a spot becomes violet then turns to deep-green again. The addition should be slow, so that the violet color does not long persist. The yield of (Z, Z)-2,4-hexadienedinitrile decreases drastically if the addition is too fast.

7. The reaction is slightly exothermic, but no precaution is necessary for a small-scale experiment. It is advisable to cool the flask in a water bath when a large-scale synthesis is carried out.

8. As both layers are black and the interface is not easy to distinguish, careful separation is necessary. In addition, black amorphous material forms at the interface, making the separation difficult. It can be coagulated by standing or removed by filtration.

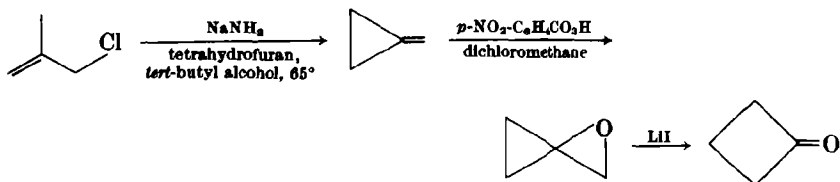
9. The infrared spectrum (chloroform) shows bands at 2230 (medium strong), 1348, and 940 (medium) cm^{-1} . The proton magnetic resonance spectrum (chloroform-*d*) shows absorption at δ 5.73 and 7.33 (AA'XX' pattern).

3. Discussion

A practical method of synthesizing (Z, Z)-2,4-hexadienedinitrile is the oxidative cleavage of 1,2-benzenediamine. Various oxidizing agents such as nickel peroxide,² lead tetraacetate,³ and silver oxide⁴ are used in more than stoichiometric amounts, but the yields are below 50%. In comparison, the present method described by Takahashi, Kajimoto, and Tsuji⁵ gives a very high yield and requires less than a stoichiometric quantity of cuprous chloride. This procedure can also be applied satisfactorily to the preparation of mucononitrile derivatives from 1,2-benzenediamines substituted with an electron-donating group, but no reaction takes place with the derivatives substituted with an electron-withdrawing group.

1. Faculty of Engineering, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152, Japan.
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CYCLOBUTANONE FROM METHYLENECYCLOPROPANE via OXASPIROPENTANE



Submitted by J. R. SALAUN, J. CHAMPION, and J. M. CONIA¹
 Checked by Ž. STOJANAC and Z. VALENTA

1. Procedure

Caution! The preparation of methylenecyclopropane must be carried out in an efficient hood because ammonia is evolved. The preparation and handling of oxaspiropentane should be carried out behind a safety screen.

A. *Methylenecyclopropane* (Note 1). A dry 3-l., three-necked, round-bottomed flask with ground-glass fittings is equipped with a sealed stirrer (Note 2) driven by a heavy-duty motor, an efficient condenser provided with a silica gel drying tube, and a 500-ml. pressure-equalizing dropping funnel connected at the top with a nitrogen inlet. The flask is charged with 450 g. (11.46 moles) of sodium amide (Note 3) and 750 ml. of anhydrous tetrahydrofuran (Note 4). The dropping funnel is charged with a solution of 283.5 g. (3.82 moles) of anhydrous *tert*-butyl alcohol (Note 5) and 300 ml. of anhydrous tetrahydrofuran. While the suspension of sodium amide is stirred vigorously under a nitrogen atmosphere, the solution of *tert*-butyl alcohol is added dropwise at room temperature during three hours. Then the stirred resulting mixture is heated to 45° with an oil bath for 2 hours. It may be necessary to add additional tetrahydrofuran at this point (Note 6). The outlet of the condenser is connected by means of an adapter to a 250-ml. gas washing bottle containing 100 ml. of 5*N* sulfuric acid to eliminate the evolved ammonia (Note 7). A silica gel drying tube (15 cm. long) joins the gas washing bottle to a 300 -ml. cold trap protected from the atmosphere with a calcium chloride drying tube and cooled in a methanol-dry ice bath maintained at -80° (Note 8). A solution of 228 g. (2.52 moles) of methallyl chloride [Propene, 2-methyl-3-chloro-]

(Note 9) in 500 ml. of dry tetrahydrofuran is added to the stirred basic mixture heated to 65° over a period of approximately 8 hours; a light nitrogen stream is used to carry the methylenecyclopropane into the cold trap. After the addition is complete, the reaction mixture is stirred and heated to 65° for 3 more hours (Note 10). The trap flask contains 58 g. (43%) of methylenecyclopropane (Note 11).

B. Oxaspiropentane. In a 3-l., three-necked, round-bottomed flask equipped with a sealed stirrer, a thermometer, and an efficient condenser cooled by methanol-dry ice (Note 12) are placed 450 ml. of dichloromethane and 200 g. (1.09 moles) of 4-nitroperbenzoic acid (Note 13). Into the mixture, stirred and cooled to -50° by immersion of the flask in a methanol-dry ice bath, 58 g. (1.07 moles) of methylenecyclopropane is distilled directly by means of a gas-inlet tube reaching to the bottom of the flask. The cooling bath is removed so that the temperature gradually rises. At about 0° the exothermic reaction starts. The temperature is maintained below 20° by occasional immersion of the flask in an ice-water bath; the methylenecyclopropane is allowed to reflux slowly (Note 14). After refluxing stops, the stirring mixture is maintained overnight at room temperature. The 4-nitrobenzoic acid is removed by filtration and the solid washed twice with 100-ml. portions of dichloromethane. The combined organic layers, which still contain about 10% of the total amount of 4-nitrobenzoic acid, are distilled at room temperature under reduced pressure (15 mm.) to eliminate the acid completely (Note 15). The distillate is then concentrated by distillation of about 450 ml. of dichloromethane through a 15-cm., helix-packed, vacuum-insulated column at a maximum oil bath temperature of 60° (Note 16).

C. Cyclobutanone (Note 16). The residue consisting of oxaspiropentane (35%) and dichloromethane (about 200 ml.) is added dropwise at room temperature to a magnetically stirred solution containing about 5-10 mg. of lithium iodide in 50 ml. of dichloromethane (Notes 17, 18), at such a rate as to maintain gentle reflux of the solvent. At the end of the addition when the reaction mixture returns to room temperature, the transformation into cyclobutanone is complete. The dichloromethane solution is washed with 20 ml. of saturated aqueous sodium thiosulfate and with 20 ml. of water. After drying over magnesium sulfate and concentration by distillation of the solvent through a 15-cm., helix-packed, vacuum-insulated column, the residual liquid consists of cyclobutanone (95%) and of 3-buten-2-one and 2-methylpropenal

(5%).⁵ A final distillation at 760 mm. through a 50-cm. stainless-steel spinning band column yields 41 g. (64% from methylenecyclopropane) of pure cyclobutanone (b.p. 100–101°) (Notes 19, 20).

2. Notes

1. The procedure described for the synthesis of methylenecyclopropane is patterned after the method reported by Caubere and Coudert.² Methylenecyclopropane is also available from the stepwise method described by Köster and co-workers.³

2. The checkers used a stirrer for vacuum work (Teflon bearing, Fisher Scientific Company). The submitters used a mercury-sealed stirrer.

3. The submitters used sodium amide (obtained from Fluka A G as small lumps under kerosene) which was washed with anhydrous tetrahydrofuran and ground with a mill. The checkers used freshly opened and recently purchased cans of sodium amide powder (Fisher Scientific Company); older reagent gave unsatisfactory results.

4. Tetrahydrofuran is purified by distillation from lithium aluminium hydride after 48 hours of refluxing over potassium hydroxide (see *Org. Syn.*, **46**, 105 (1966)).

5. *tert*-Butyl alcohol is refluxed overnight over calcium hydride and distilled.

6. The checkers obtained a heavy slurry at this stage which became heavier during addition of methallyl chloride. They found it necessary to dilute with more tetrahydrofuran (about 450 ml. for the scale given in the procedure) before methallyl chloride was added.

7. It is advisable to insert a safety bottle to avoid any run-back of sulfuric acid into the reaction flask. The gas washing bottle must be cooled by immersion in a large water bath (15°); the sulfuric acid solution is replaced by a fresh 5*N* solution when neutralized by evolved ammonia (checked by phenolphthalein).

8. Methylenecyclopropane, b.p. 11° (760 mm.), is volatile at room temperature; all adapter fittings must be carefully checked. The checkers recommend the use of two cold traps in series.

9. 3-Chloro-2-methylpropene (methallyl chloride) is available from Fluka A G and Eastman Organic Chemicals. The chloride, b.p. 72° (760 mm.), was distilled before use.

10. In the checkers' hands, at least 24 hours was needed to produce

the bulk of methylenecyclopropane; small amounts of the product condensed during an additional 24-hour period.

11. The yield is determined by weighing the cold trap before and after distillation of methylenecyclopropane. Any small amounts of tetrahydrofuran carried into the methylenecyclopropane trap are eliminated in a subsequent distillation. By proton magnetic resonance analysis the checkers found that no tetrahydrofuran reached the cold traps; the spectrum (dichloromethane) shows a triplet at δ 1.00 and a quintuplet at δ 5.35 in the ratio 4:2.

12. *Caution! The yield isolated from this reaction depends on the efficiency of this condenser; the epoxidation is exothermic and methylenecyclopropane is volatile.*

13. The 4-nitroperbenzoic acid (98–99%) is available from K and K Laboratories and Prolabo (France) or may be prepared from 4-nitrobenzoic acid as described.⁴

14. Cooling below 0° stops the reaction.

15. A short-path distillation apparatus is used, the distillate (oxaspiropentane plus dichloromethane) being trapped in a receiver placed in a methanol–dry ice bath cooled to –80°. The checkers found it useful to drive out last traces of product by adding several milliliters of dichloromethane to the residual thick paste and distilling. The proton magnetic resonance spectrum (dichloromethane) shows an octet at δ 0.85 and a singlet at δ 3.00 in the ratio 4:2.

16. If the oil bath temperature reaches 80°, the residue consists of cyclobutanone (75%) and oxaspiropentane (25%). Distillation of this residue at 97–103° (760 mm.) yields cyclobutanone and oxaspiropentane.

17. *Caution! Addition of lithium iodide (catalytic amount) to a dichloromethane solution containing more than 30% oxaspiropentane leads to a very vigorous reaction.*

18. Dichloromethane from the previous distillation is used.

19. The purity of cyclobutanone was checked by gas chromatography on a 3.6-m. column containing 20% silicone SE 30 on chromosorb W at 65°. The infrared spectrum (neat) shows carbonyl absorption at 1779 cm^{-1} ; the proton magnetic resonance spectrum (carbon tetrachloride) shows a multiplet at δ 2.00 and a triplet at δ 3.05 in the ratio 1:2.

20. The checkers obtained yields of 61–64% on smaller-scale runs (~10 g. of cyclobutanone).

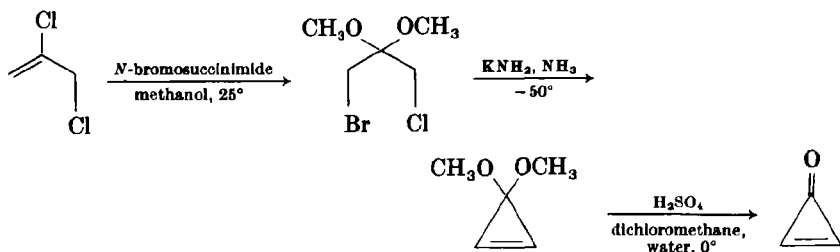
3. Discussion

This method for the preparation of cyclobutanone *via* oxaspiropentane is an adaptation of that described by Salaün and Conia.⁵ The previously known large-scale preparations of cyclobutanone consist of the reaction of the hazardous diazomethane with ketene,⁶ the oxidative degradation⁷ or the ozonization in presence of pyridine⁸ of methylenecyclobutane prepared from pentaerythritol, or the recently reported dithiane method of Corey and Seebach,⁹ which has the disadvantage of producing an aqueous solution of the highly water-soluble cyclobutanone. A procedure involving the solvolytic cyclization of 3-butyne-1-yl trifluoromethanesulfonate is described in *Org. Syn.*, **54**, 84 (1974).

The procedure described here is a large-scale preparation with satisfactory yields of a still very expensive but simple compound from very cheap and readily available starting materials and with ordinary laboratory equipment. This rearrangement of oxaspiropentanes into cyclobutanones appears to be general for the preparation of substituted cyclobutanones.¹⁰

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CYCLOPROPENONE



Submitted by R. BRESLOW, J. PECORARO, and T. SUGIMOTO¹
 Checked by R. LÜTHI, H. WÜEST, and G. BÜCHI

1. Procedure

Caution! Because liquid ammonia is used in Part B, this part of the procedure should be conducted in a well-ventilated hood.

A. 1-Bromo-3-chloro-2,2-dimethoxypropane. In a good hood, a 1-l., three-necked, round-bottomed flask equipped with magnetic stirrer and reflux condenser is charged with 300 ml. of anhydrous methanol, 111 g. (1.0 mole) of 2,3-dichloro-1-propene (Note 1), and a few drops of concentrated sulfuric acid. *N*-Bromosuccinimide (178 g., 1.0 mole) is added in small portions through the condenser with stirring. After the final addition, the reaction mixture is stirred for another hour at room temperature, and 5 g. of anhydrous sodium carbonate is then added to neutralize the catalyst. The solution is stirred for 15 minutes longer and then poured into a large separatory funnel containing 300 ml. of water. The lower, organic layer is removed, and the aqueous layer is extracted with two 500-ml. portions of pentane. The combined organic extracts are washed twice with an equal volume of water, dried over anhydrous magnesium sulfate, filtered, and evaporated to give a white semi-crystalline mass. This is dissolved in refluxing pentane (250 ml.), and the solution is cooled in an acetone-dry ice bath for 30 minutes to yield 89–99 g. (41–45%) of the white crystalline ketal, m.p. 69.5–70.5° (Note 2).

B. 3,3-Dimethoxycyclopropene. A 500-ml., three-necked, round-bottomed flask is equipped with a magnetic stirrer, a gas-inlet tube, a thermometer, and an acetone-dry ice condenser charged with acetone–

dry ice and topped with a drying tube containing sodium hydroxide pellets. An acetone-dry ice bath is placed under the flask, and ammonia is condensed into the flask from a commercial cylinder. When 350–400 ml. of ammonia has condensed, the inlet tube is replaced by a stopper, and a small piece (0.5 g.) of potassium metal is added to the ammonia. The cooling bath is removed, and *ca.* 0.05 g. of anhydrous ferric chloride is added. When the ammonia reaches reflux temperature, the blue color of the dissolved potassium turns to gray, and the remainder of the potassium (11.7 g., 0.30 g.-atom total) is added in 0.5-g. pieces at such a rate that a gentle reflux is maintained. The stopper is then replaced by an addition funnel containing a solution of 1-bromo-3-chloro-2,2-dimethoxypropane (21.7 g., 0.10 mole) in 50 ml. of anhydrous ether. This solution is added to the gray potassium amide-ammonia suspension over a period of 15 minutes, during which time the mixture is maintained at -50° to -60° by use of the cooling bath (Note 3). After 3 hours at this temperature, solid ammonium chloride (10.8 g., 0.20 mole) is added with stirring. Ammonia is allowed to evaporate by removing the cooling bath, and during the course of the evaporation it is replaced with 350 ml. of anhydrous ether. When the reaction temperature reaches *ca.* 0° , the resulting brown solution is filtered from inorganic salts and placed in a 500-ml., round-bottomed flask (Note 4). The ethereal solution is then subjected to reduced pressure (50–80 mm.), vacuum being applied through a dry-ice condenser charged with carbon tetrachloride-dry ice (*ca.* -25°), while the flask is immersed in an ice bath. After 4–5 hours, when the quantity of residue seems to remain constant, the dry-ice condenser is replaced by a distilling head. The pressure is decreased to 1–2 mm., and a clear liquid is collected by distillation into a receiver maintained in a cooling bath at -78° . The product, 3,3-dimethoxycyclopropene, is obtained in a quantity of 4–6.5 g. (40–65% yield) (Note 5). This material has been purified further,² but it can be used directly in the next step. If it is stored, it should be kept below 0° .

C. *Cyclopropenone*. To a stirred solution of 3.0 g. (0.030 mole) of 3,3-dimethoxycyclopropene in 30 ml. of dichloromethane at 0° is added dropwise 5 ml. of cold water containing 3 drops of concentrated sulfuric acid. The reaction mixture is stirred at 0° for an additional 3 hours. Then 30 g. of anhydrous sodium sulfate is added in portions to the solution with stirring at 0° . The drying agent is removed by filtration, and the solvent is evaporated at 50–80 mm. with a water bath maintained at $0-10^{\circ}$. The brown, viscous residue is then distilled at 1–2 mm. With the

bath temperature at 10°, the distillate collected in a receiver cooled to -78° is a mixture of methanol and dichloromethane. A new receiver is attached, and the bath temperature is gradually raised to 35° (Note 6), whereupon cyclopropenone collects in the receiver as a white solid. The yield is 1.42–1.53 g. (88–94%). The compound has b.p. 26° (0.46 mm.) and m.p. -29° to -28° (Note 7).

Cyclopropenone prepared in this way is quite pure and suitable for most chemical purposes. It can be repurified by crystallization from 3 volumes of ethyl ether at -60° using a cooled filtering apparatus. The residual ethyl ether is then removed by evaporation at 1–2 mm. and 0°; very pure cyclopropenone is obtained in 60–70% recovery from the above distilled material.

2. Notes

1. Commercial material was used without further purification. The reflux condenser is used to decrease evaporative losses of this material.

2. Proton magnetic resonance (carbon tetrachloride) δ (number of, protons, multiplicity): 3.63 (2, singlet), 3.48 (2, singlet), 3.27 (6, singlet). The infrared and mass spectra are also as reported.²

3. Any crystals which may form at the tip of the addition funnel are scraped off and allowed to drop into the reaction flask.

4. The checkers found it inconvenient to complete Part B in one day, and thus they stored this ethereal solution overnight in the freezer compartment of a refrigerator.

5. The product usually contains small amounts of ether, as judged by proton magnetic resonance. The yields given are based on pure cyclopropenone ketal. Proton magnetic resonance (chloroform-*d*) δ (number of protons, multiplicity): 7.88 (2, singlet), 3.33 (6, singlet).

6. The bath temperature should be raised slowly to prevent decomposition of cyclopropenone.

7. Infrared (chloroform) cm.^{-1} : 1870, 1840, 1493; proton magnetic resonance (chloroform-*d*) δ : 9.11 (singlet).

3. Discussion

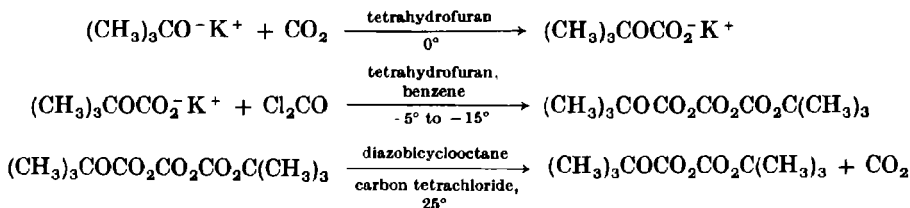
Cyclopropenone was first synthesized³⁻⁵ by the hydrolysis of an equilibrating mixture of 3,3-dichlorocyclopropene and 1,3-dichlorocyclopropene (prepared by reduction of tetrachlorocyclopropene with tributyltin hydride). This procedure has been adapted^{5,4} to prepare

labeled and deuterated cyclopropanone for physical studies. The current procedure is somewhat more convenient. It is closely based on the work of Baucom and Butler,² who have described this synthesis of dimethoxycyclopropene and shown that this ketal can be hydrolyzed to cyclopropanone. The isolation of pure cyclopropanone by hydrolysis of the ketal is parallel to the Breslow and Oda procedure⁵ for its isolation by hydrolysis of the dichlorocyclopropenes.

Cyclopropanone is a molecule of considerable theoretical interest, since it combines remarkable stability with extreme strain. Various physical studies⁶ suggest that much of its stability is derived from the special conjugative stabilization in a two- π -electron system which is related to the cyclopropenyl cation. In addition, cyclopropanone has a number of interesting chemical properties^{7,8} which suggest that it could be a useful synthetic intermediate. It has been used in the synthesis of cyclopropanone derivatives⁷ and of tropones,⁷ the latter by rearrangement of products derived from Diels–Alder reactions. In addition, it undergoes a very interesting cyclization–rearrangement reaction with diazo compounds which leads to the overall insertion of three carbons between the diazo group and its original attachment point.⁷ Perhaps the most remarkable reaction of cyclopropanone so far reported is its conversion with Grignard reagents into 2-substituted resorcinols.⁸ This reaction seems to be of some generality, and it represents a simple way to elaborate a resorcinol ring (all six carbons of the resorcinol system are derived from two molecules of cyclopropanone) onto a variety of alkyl groups. The ready availability of this compound should lead to other synthetic applications.

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DI-*tert*-BUTYL DICARBONATE
[Dicarbonic acid, di-*tert*-butyl ester]



Submitted by BARRY M. POPE, YUTAKA YAMAMOTO,
 and D. STANLEY TARBELL¹
 Checked by JOHN C. DuBOSE and HERBERT O. HOUSE

1. Procedure

Caution! Since the toxic gas phosgene is employed in this preparation, the reaction should be performed in an efficient hood. The glassware, which may be coated with a solution of phosgene, should be washed before it is removed from the hood.

A. Di-*tert*-butyl tricarbonat. A 1-l., three-necked flask, fitted with a mechanical stirrer, a 200-ml. pressure-equalizing dropping funnel, a calcium chloride-filled drying tube, and gas-inlet tube with a minimum internal diameter of 6 mm. (Note 1) extending nearly to the bottom of the flask, is dried either by heating with a free flame while passing anhydrous nitrogen through the apparatus or by heating to 120° for several hours in an oven. Before use, the dropping funnel should be calibrated to indicate levels corresponding to 85 ml. and 105 ml. of liquid. While an atmosphere of anhydrous nitrogen (Note 2) is maintained inside the apparatus, it is allowed to cool and then a mixture of 44.8 g. (0.40 mole) of alcohol-free potassium *t*-butoxide (Note 3) and 550 ml. of anhydrous tetrahydrofuran (Note 4) is added to the reaction flask. The resulting mixture is stirred under an atmosphere of anhydrous nitrogen for 5–10 minutes to obtain a solution (Notes 3, 5). The reaction flask is immersed in an ice-salt bath maintained at –5° to –20°, and all subsequent steps, including solvent removal, are performed with this cooling bath in place. A stream of anhydrous carbon dioxide (Note 2) is passed through the cold reaction solution for 30 minutes with

vigorous stirring. This addition of carbon dioxide results in the formation of a thick, creamy slurry in the reaction flask. While the reaction mixture is being saturated with carbon dioxide, 85 ml. of anhydrous benzene should be added to the dropping funnel and then a stream of phosgene should be bubbled through the benzene until the total volume of the phosgene solution in benzene is 105 ml., corresponding to the addition of approximately 24 g. (0.24 mole) of phosgene (Note 6). When the addition of carbon dioxide is complete, the solution of phosgene in benzene is then added to the cold reaction slurry, dropwise and with vigorous stirring during 1 hour, while the temperature of the cooling bath is maintained at -5° to -15° . During this addition the reaction mixture becomes less viscous but remains as a white slurry. When the addition of the phosgene solution is complete, the resulting cold reaction mixture is stirred for an additional 45 minutes while a stream of anhydrous nitrogen is passed through the reaction solution to sweep out most of the excess phosgene. Then the fittings are removed from the reaction flask, two of the three necks are stoppered, and the volume of solvents in the reaction flask is reduced from about 650 ml. to 100 ml. by evaporation under reduced pressure with a rotary evaporator. During this evaporation of solvents the flask should be continuously cooled in an ice-salt bath maintained at -5° to 0° . This evaporation should be performed with either a very efficient aspirator or with a mechanical vacuum pump fitted with an efficient cold trap. Since some phosgene is still present in the reaction mixture, the exhaust from the aspirator or the vacuum pump should be discharged in the hood and any material collected in a cold trap should be emptied in the hood. The residual slurry of finely divided potassium chloride is filtered with suction in a large-diameter, fritted-glass funnel that has been precooled with 50 ml. of ice-cold pentane. During this filtration the filter funnel may be loosely covered with an inverted large-diameter funnel through which a stream of nitrogen is passed to protect the contents of the funnel from atmospheric moisture. The residue in the reaction flask should be washed into the filter funnel with 350 ml. of ice-cold pentane. Then the residue in the filter funnel is washed with two additional 100-ml. portions of ice-cold pentane to leave the white potassium chloride as a residue. The combined filtrate and pentane washings are then concentrated to dryness at 0° employing a rotary evaporator with the reduced pressure supplied by a mechanical vacuum pump equipped with an efficient cold trap. The residual colorless solid product, di-*tert*-butyl tricarbonat, amounts

to 33.7–39.6 g. (64–75%, Note 7). This crude product is recrystallized from pentane by dissolving the crude product in 1250 ml. of pentane at room temperature and then cooling the solution to -15° . The pentane mother liquors are concentrated with a rotary evaporator to separate two additional crops of crystalline product. The total yield is 31.2–32.8 g. (59–62%) of the pure di-*tert*-butyl tricarboxylate as colorless prisms, m.p. $62-63^{\circ}$ dec. (Note 8).

B. *Di-tert-butyl dicarbonate*. A solution of 20.0 g. (0.076 mole) of di-*t*-butyl tricarboxylate in 75 ml. of carbon tetrachloride is placed in a 600-ml. beaker fitted with a magnetic stirrer, and 0.10 g. (0.0009 mole) of freshly sublimed 1,4-diazabicyclo[2.2.2]octane (DABCO) is added (Note 9). Rapid evolution of carbon dioxide begins at once. The reaction mixture is stirred at 25° for 45 minutes to complete the loss of carbon dioxide (Note 10), and then 35 ml. of water, containing sufficient citric acid to make the aqueous layer slightly acidic, is added. The layers are separated and the organic layer is dried over anhydrous magnesium sulfate and then concentrated at 25° with a rotary evaporator. The residual liquid is distilled under reduced pressure to separate 13.3–15.1 g. (80–91%) of di-*tert*-butyl dicarbonate as a colorless liquid, b.p. $55-56^{\circ}$ (0.15 mm.) or $62-65^{\circ}$ (0.4 mm.) n_D^{25} 1.4071–1.4072 (Note 11).

2. Notes

1. A gas-inlet tube of smaller diameter or a tube fitted with a fritted-glass outlet tends to become clogged during this preparation and is not recommended.

2. The submitters dried this gas by passing it successively through an empty trap, through a trap containing concentrated sulfuric acid, and through another empty trap. The checkers used this drying procedure for carbon dioxide but dried the nitrogen by passing it through a column of molecular sieves.

3. The submitters employed alcohol-free potassium *tert*-butoxide, purchased from K & K Laboratories, without further purification; the checkers employed comparable material taken from a freshly opened bottle purchased from MSA Research Corporation. The submitters report that among approximately ten different bottles of commercial potassium *tert*-butoxide used, only material from one bottle failed to form the tricarboxylate in this procedure. The defective material in this one bottle was an extremely fine powder that failed to dissolve when

stirred with tetrahydrofuran. Solubility in tetrahydrofuran appears to be a good criterion for the purity of alcohol-free potassium *tert*-butoxide. The checkers have observed that the 1:1 complex of potassium *tert*-butoxide and *tert*-butyl alcohol is much less soluble in etheral solvents than is alcohol-free potassium *tert*-butoxide.

4. A reagent grade of tetrahydrofuran (b.p. 65–66°) was distilled from lithium aluminum hydride before use.

5. The submitters reported that their solution had a faint blue color at this point.

6. If desired, the dropping funnel may be removed from the reaction flask and replaced with a calcium chloride-filled drying tube during the preparation of the phosgene solution. When preparation of the phosgene solution is complete, the drying tube should be removed and quickly replaced with the dropping funnel containing the phosgene solution.

7. Although the submitters report that this crude product is suitable for use in the next step of this preparation, the checkers found that once when using the crude product the subsequent reaction did not go to completion unless an extra quantity of the diamine base was added. This suggests that some potentially acidic impurity such as *tert*-butyl chloroformate may be present in the crude product and could interfere with the subsequent reaction. The checkers therefore recommend that the product be purified before use in the next step of this preparation.

8. Although this tricarbonatc undergoes thermal decomposition when heated above its melting point (63°) to form *tert*-butyl alcohol, isobutylene, and carbon dioxide, the product appears to be stable to storage at temperatures of 25° or less. The product exhibits infrared bands (carbon tetrachloride) attributable to C=O stretching at 1845, 1810, and 1780 cm^{-1} ; the proton magnetic resonance spectrum (carbon tetrachloride) exhibits a singlet at δ 1.55.

9. The submitters report that both 1,4-diazabicyclo[2.2.2]octane and triethylamine have been used to catalyze this decomposition. Triethylamine was less satisfactory as a catalyst because of its relatively rapid reaction with the solvent, carbon tetrachloride, to form triethylamine hydrochloride and because of difficulty encountered in separating triethylamine from the dicarbonate product. The 1,4-diazabicyclo[2.2.2]octane was efficiently separated from the dicarbonate product by the procedure described in which the crude product was washed with very dilute aqueous acid.

10. The progress of this reaction may be followed either by observing the disappearance of the band at 1845 cm^{-1} in the infrared or by following the replacement of the reactant proton magnetic resonance peak (carbon tetrachloride) at $\delta\ 1.55$ by the product peak at $\delta\ 1.50$.

11. The submitters report that this product solidifies when cooled and melts at $21\text{--}22^\circ$ and that the product is stable when stored in a refrigerator. The product exhibits infrared absorption (carbon tetrachloride) attributable to $\text{C}=\text{O}$ stretching at 1810 and 1765 cm^{-1} and a proton magnetic resonance singlet at $\delta\ 1.50$ (carbon tetrachloride). The mass spectrum of the product exhibits the following relatively abundant fragment peaks: m/e (relative intensity), $60(10)$, $59(99)$, $57(34)$, $56(86)$, $55(47)$, $50(21)$, $44(100)$, $43(30)$, $41(91)$, $40(27)$, and $39(61)$.

3. Discussion

Di-*tert*-butyl tricarboxylate, an example of hitherto unknown class of compounds, has been prepared only by the present procedure.²⁻⁴ The corresponding sulfur compound, $t\text{-C}_4\text{H}_9\text{SCO}_2\text{CO}_2\text{COS-}t\text{-C}_4\text{H}_9$, is also a new class of compound that has been prepared by a similar procedure in comparable yields.^{4,5} Both of these tricarboxylates are smoothly converted by basic catalysts into the corresponding dicarbonates (sometimes called pyrocarbonates); kinetics and differences in thermal decomposition of both tricarboxylates have been reported as well as other reactions of these materials.^{4,6} The amine-catalyzed decomposition of the tricarboxylates to form dicarbonates is believed to involve initial nucleophilic attack by the amine at the center carbonyl group of the tricarboxylate.^{4,6} Di-*tert*-butyl dicarbonate had been obtained previously⁷ in 5% yield; no study of its properties was reported.⁷ The di-*tert*-butyl dicarbonate and its sulfur analog have been shown to react with amino acids and their derivatives to form the corresponding *N-tert*-butoxycarbonyl (*t*-BOC) and *N-tert*-butylthiocarbonyl derivatives,³ which are valuable protecting groups for amino groups. The dicarbonates described in the present synthesis are very mild reagents for the preparation of *t*-BOC and *N-tert*-butylthiocarbonyl derivatives, and may have application in selective reactions with enzymes, nucleic acids and their component nucleotides and nucleosides. Diethyl dicarbonate has been extensively studied in reactions of this type.^{8,9}

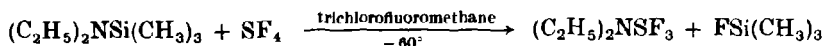
Other reagents which have been found useful for the synthesis of *t*-BOC derivatives include the hazardous *tert*-butoxycarbonyl azide¹⁰

(see warning, p. 122), *tert*-butyl phenyl carbonate,¹¹ and 2-*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile.¹²

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DIETHYLAMINOSULFUR TRIFLUORIDE

[Sulfur, (diethylamino)trifluoro-]



Submitted by W. J. MIDDLETON and E. M. BINGHAM¹
 Checked by RONALD F. SIELOFF, EUGENE R. KENNEDY,
 and CARL R. JOHNSON

1. Procedure

Caution! This procedure should be conducted in a good hood to avoid exposure to sulfur tetrafluoride. Protective gloves should be worn when handling diethylaminosulfur trifluoride since this material can cause severe HF burns.

A dry 1-l., three-necked, round-bottomed flask is equipped with a thermometer (-100° to 50°), a magnetic stirrer, and two dry-ice condensers (one condenser is capped with a drying tube, the other with a

gas-inlet tube). The apparatus is flushed with dry nitrogen, and 300 ml. of trichlorofluoromethane (Note 1) is added to the flask. As the nitrogen atmosphere is maintained, the trichlorofluoromethane is cooled to -70° by means of a acetone-dry ice bath and 119 g. (1.1 moles) of sulfur tetrafluoride (Note 2) is added from a cylinder through the gas-inlet tube (Note 3). The gas-inlet tube is then replaced with a 250-ml., pressure-equalized dropping funnel charged with a solution of 145 g. (1 mole) of *N,N*-diethylaminotrimethylsilane (Note 4) in 90 ml. of trichlorofluoromethane. This solution is added dropwise, with stirring, to the sulfur tetrafluoride solution at a rate slow enough to keep the temperature of the reaction mixture below -60° (about 40 minutes). The cooling bath is removed, and the reaction mixture is allowed to warm spontaneously to room temperature. The apparatus is arranged for distillation with a simple distillation head, and the solvent (b.p. 24°) and by-product fluorotrimethylsilane (b.p. 17°) are distilled into a well-cooled receiver by warming the reaction mixture gently to 45° by means of a heating mantle. The yellow to dark-brown residual liquid is transferred and distilled at reduced pressure through a spinning-band column to give 131 g. (81%) of diethylaminosulfur trifluoride as a light yellow liquid, b.p. $46-47^{\circ}$ (10 mm.) (Note 5). This product can be stored for several months at room temperature in an inert plastic bottle (such as a bottle made of polypropylene or Teflon FEP), or for short periods of time in a dry glass bottle.

2. Notes

1. Trichlorofluoromethane (Freon 11) is available from E. I. duPont de Nemours and Company, Inc., or Matheson Gas Products.

2. Sulfur tetrafluoride is available from Air Products and Chemicals, Inc., or Matheson Gas Products.

3. If it is inconvenient to add sulfur tetrafluoride directly from a cylinder, it may first be condensed in a calibrated trap containing a boiling chip and cooled in a acetone-dry ice bath. When cooled to -78° , 119 g. of sulfur tetrafluoride is about 62 ml. The sulfur tetrafluoride can be added to the cooled flask by allowing it to distil slowly from the trap.

4. *N,N*-Diethylaminotrimethylsilane is available from PCR, Inc., or it can be prepared by the following procedure. A solution of 292 g. (413 ml.) of diethylamine in 1000 ml. of diethyl ether is cooled in an ice

bath, and a solution of 216 g. (252 ml.) of chlorotrimethylsilane in 200 ml. of diethyl ether is added dropwise with mechanical stirring over a period of 1 hour. The precipitated solid is removed by filtration, thoroughly washed with ether, and the filtrate is fractionally distilled to give 175 g. (60%) of *N,N*-diethylaminotrimethylsilane as a colorless liquid, b.p. 124–125°.

5. The reaction of diethylaminosulfur trifluoride with water is highly exothermic; clean-up procedures should be carried out with caution.

3. Discussion

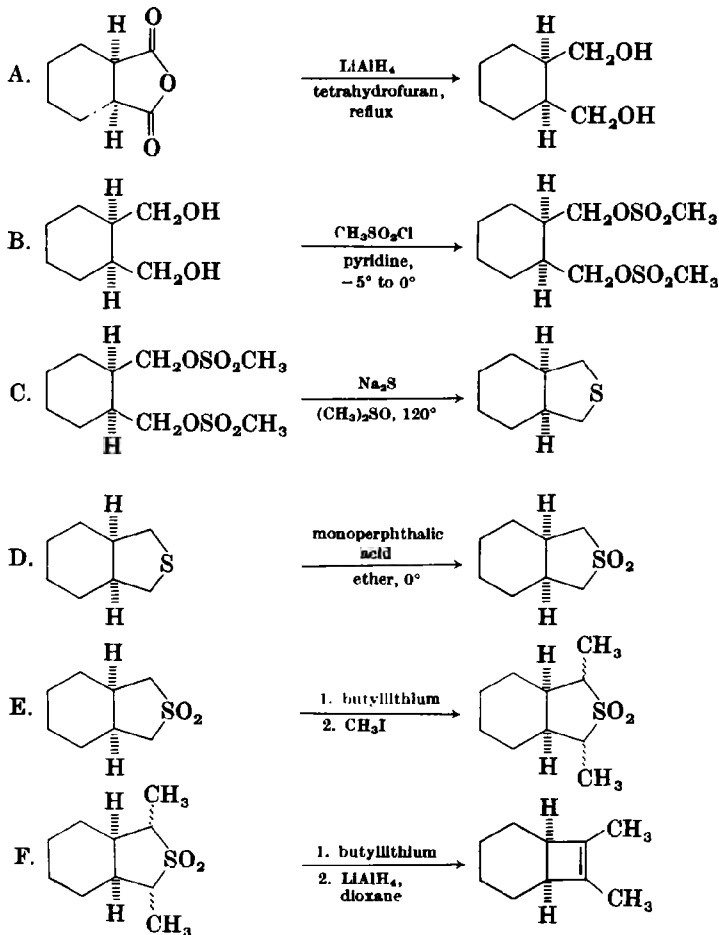
Diethylaminosulfur trifluoride is a useful and convenient reagent for replacing primary, secondary, and tertiary hydroxyl and aldehyde and ketone carbonyl oxygen^{2,3} with fluorine, even in the presence of other halogens and other functional groups, such as carboxylic esters. In contrast to sulfur tetrafluoride, this reagent is a liquid that can be easily measured and used in standard glass equipment at moderate temperatures and atmospheric pressure, and can be used on acid-sensitive compounds (such as pivaldehyde) to convert them into the fluorinated derivative. In contrast to other reagents such as SF₄, SeF₄·pyridine HF, HF·pyridine, and (C₂H₅)₂NCF₂CFHCl, this reagent can replace OH groups with F in primary alcohols such as isobutyl alcohol without causing extensive rearrangement or dehydration.

This preparation of diethylaminosulfur trifluoride is an adaptation of a procedure first described by von Halasz and Glemser.⁴ The same procedure can also be used to prepare other dialkylaminosulfur trifluorides by the substitution of the diethylaminotrimethylsilane with other dialkylaminotrimethylsilanes.²

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**1,2-DIMETHYLCYCLOBUTENES BY REDUCTIVE RING-
CONTRACTION OF SULFOLANES: *cis*-7,8-DIMETHYLBICYCLO-
[4.2.0]OCT-7-ENE**

[Bicyclo[4.2.0]oct-7-ene, *cis*-7,8-dimethyl-]



Submitted by JAMES M. PROTIS
and LEO A. PAQUETTE¹

Checked by C.-P. MAX and G. BÜCHER

1. Procedure

Caution! Steps B and C should be performed in a hood because of the noxious odors produced.

A. *cis*-1,2-Cyclohexanedimethanol. In a 3-l., three-necked, round-bottomed flask fitted with a mechanical stirrer, addition funnel, and condenser is placed 1.5 l. of anhydrous tetrahydrofuran (Note 1). With vigorous stirring, 14.8 g. (0.39 mole) of lithium aluminum hydride is added and a solution of *cis*-1,2-cyclohexanedicarboxylic anhydride [1,3-Isobenzofurandione, *cis*-hexahydro-] (50.0 g., 0.325 mole) in 300 ml. of tetrahydrofuran is introduced in a thin stream during 30 minutes. The resulting suspension is then maintained at the reflux temperature for 3 hours by use of a heating mantle. After this time, heating is ceased and 100 ml. of a freshly prepared (Note 2), saturated aqueous sodium sulfate solution is cautiously added dropwise (Note 3). The highly granular insoluble salts, which change in appearance from gray to white, are removed by suction filtration through a Büchner funnel and washed thoroughly with ether. The combined filtrates are freed of solvent on a rotary evaporator to give 46.0–46.5 g. (98–100%) of the diol as a colorless, viscous oil which may slowly crystallize, m.p. 38–40° (Note 4). Pure *cis*-1,2-cyclohexanedimethanol is reported to have m.p. 42–43°. ²⁻⁴

B. *cis*-1,2-Cyclohexanedimethanol Dimethanesulfonate. In a 5-l., three-necked, round-bottomed flask, immersed in an ice-salt bath and fitted with a mechanical stirrer and an addition funnel, is placed a solution of 111 g. (0.97 mole) of methanesulfonyl chloride in 1.2 l. of pyridine. While cooling and stirring, a solution of 46.4 g. (0.322 mole) of *cis*-1,2-cyclohexanedimethanol in 250 ml. of pyridine is added dropwise at a rate such that the temperature does not exceed 0° (Note 5). Upon completion of the addition, the mixture is stirred at –5° to 0° for an additional 2 hours. Two liters of cold 10% hydrochloric acid is introduced at a rate which maintains the reaction mixture below 20° (Note 5). The solid which separates is isolated by suction filtration, washed sequentially with 1 l. of dilute hydrochloric acid and 2 l. of water, and air-dried. There is isolated 93–95 g. (96–98%) of the dimethanesulfonate having m.p. 66–67.5°. Recrystallization from methanol gives needles melting at 75–76° (Note 6).

C. *cis*-8-Thiabicyclo[4.3.0]nonane [*Benzo[c]thiophene cis-octahydro*]-. A 3-l., three-necked, round-bottomed flask is fitted with a mechanical

stirrer, capillary tube, heating mantle, and 90° adapter connected to a condenser and receiving flask. To the reaction vessel are added 240 g. (1.0 mole) of recrystallized sodium sulfide nonahydrate (Note 7) and 2 l. of dimethyl sulfoxide. As the mixture is stirred, the internal pressure is reduced to 30 mm., and heating is applied until 300–350 ml. of distillate is collected (Note 8). After cooling to 40°, the capillary and take-off adapter are replaced by a thermometer and condenser and 95 g. (0.316 mole) of *cis*-1,2-cyclohexanedimethanol dimethanesulfonate is introduced in one portion (Note 9). The mixture is then stirred at 120° for 18 hours, cooled, and transferred to a 5-l. separatory funnel containing 1500 g. of ice. After 1 l. of hexane is added and the two-phase mixture well shaken, the aqueous phase is reextracted with hexane (500 ml.). The combined organic layers are washed with four 1-l. portions of water, dried over anhydrous magnesium sulfate, and concentrated with a rotary evaporator. The sulfide is collected by bulb-to-bulb distillation at 0.05–0.1 mm. as a colorless liquid 30.8–31.6 g. (68.0–70.5%) (Note 10).

D. *cis*-8-*Thiabicyclo*[4.3.0]*nonane* 8,8-*Dioxide* [*Benzo*[*c*]*thiophene* 2,2-*dioxide*, *cis*-*octahydro*-]. A solution of the sulfide (43.0 g., 0.303 mole) in 1 l. of ether is cooled to 0° and treated dropwise while magnetically stirred with 1.0 l. of 0.65*N* ethereal monoperphthalic acid (0.65 mole).⁵ The mixture is kept overnight at 0°, after which time the precipitated phthalic acid is separated by filtration and the filtrate concentrated with a rotary evaporator. Bulb-to-bulb distillation of the residual oil at 0.05–0.1 mm. affords the sulfone as a colorless liquid (48.5–50 g., 92–95%) (Note 11). This product is crystallized from ether-hexane to give a colorless solid, m.p. 39–41° (Note 12).

E. 7,9-*Dimethyl-cis*-8-*thiabicyclo*[4.3.0]*nonane* 8,8-*Dioxide* [*Benzo*[*c*]-*thiophene* 2,2-*dioxide*, *cis*-*octahydro*-1,3-*dimethyl*-]. A 2-l., one-necked, round-bottomed flask is charged with 800 ml. of anhydrous tetrahydrofuran and 49.0 g. (0.281 mole) of *cis*-8-*thiabicyclo*[4.3.0]*nonane* 8,8-*dioxide*. The solution is blanketed with nitrogen and the flask is fitted with a side-arm adapter having a nitrogen inlet and a rubber septum. The contents are cooled in a 2-propanol–dry ice bath and 225 ml. of 2.5 *M* butyllithium in hexane (0.562 mole) is introduced by syringe (Notes 13, 14). After 5–10 minutes, 142 g. (1.0 mole) of methyl iodide is added in similar fashion and the cooling bath is removed. Upon warming to room temperature, the reaction mixture is treated slowly with 1 l. of water followed by 1 l. of ether, and the organic layer is separated,

washed once with 1 l. of water, dried over anhydrous magnesium sulfate, and evaporated under reduced pressure. The resulting pale-yellow oil (49.5–51 g., 87–89.5%), which consists of a mixture of isomers, is not further purified.

F. *cis*-7,8-*Dimethylbicyclo*[4.2.0]*oct*-7-*ene*. A 1-l., one-necked, round-bottomed flask is charged with 50.5 g. (0.25 mole) of the sulfone from Part E and 200 ml. of dry dioxane (Note 15). The solution is blanketed with nitrogen and the flask is fitted with a side-arm adapter having a nitrogen inlet and a rubber septum. With ice cooling and magnetic stirring, 150 ml. of 2.5 *M* butyllithium in hexane (0.375 mole) is added by syringe (Notes 13, 14). The resulting yellow-orange inhomogeneous mixture is transferred under nitrogen to a 500-ml. pressure-equalizing dropping funnel and introduced during 25 minutes to a stirred refluxing mixture of lithium aluminum hydride (32.0 g., 0.843 mole) and 2 l. of dry dioxane (Notes 16, 17). Upon completion of the addition, the contents are heated at the reflux temperature with a mantle for 20 hours, whereupon 100 ml. of saturated aqueous sodium sulfate solution is added dropwise with cooling (Note 18). The precipitated solids are separated by filtration and washed repeatedly with hexane (Note 19). The combined filtrates are diluted with an additional liter of hexane and washed with four 1-l. portions of water. The organic phase is dried over anhydrous sodium sulfate and carefully concentrated with a rotary evaporator. The residual cyclobutene is purified by distillation to give 10.0–12.5 g. (29.5–37%) of colorless oil, b.p. 63–65° (33 mm.) (Notes 20, 21).

2. Notes

1. The tetrahydrofuran used in these preparations was distilled from lithium aluminum hydride.

2. A sodium sulfate solution which is not freshly prepared ultimately gives a precipitate of small particle size that is exceedingly difficult and tedious to separate by vacuum filtration.

3. Because the initial reaction is extremely vigorous and exothermic, the first few milliliters must be added very cautiously. In the more advanced stages of this addition the rate of flow may be judiciously increased.

4. Recrystallization of this material from benzene-light petroleum ether gives a pure product of m.p. 42–43°.

5. This reaction is significantly exothermic. Stronger cooling as from an acetone-dry ice bath can be employed if desired to expedite the addition of diol. In any event, a temperature in excess of 20° leads to unwanted rapid hydrolysis and formation of water-soluble by-products.

6. This dimethanesulfonate is reported to have m.p. 75–76°.³

7. Sodium sulfide may be conveniently recrystallized from ethanol. Unrecrystallized material may be utilized. However, significantly lower yields will result if the ensuing minor modification is not followed.

8. If unpurified sodium sulfide is employed, a significant quantity of dark insoluble material is seen to adhere to the walls of the flask. Removal of these unwanted contaminants is readily effected by decantation of the hot solution into a second 3-l., three-necked flask before crystallization begins.

9. An exotherm is witnessed and the temperature rises to 70–80°. A color change from yellow to deep purple is also seen; the extent of coloration varies with the purity of the sodium sulfide nonahydrate.

10. The submitters report a yield of 42.0–43.5 g. (93.5–96.8%). The checkers could not reproduce these results in three attempts.

This sulfide has also been prepared from the corresponding dibromide.⁶

11. The checkers performed this step on a smaller scale (*ca.* $\frac{2}{3}$) and noted (proton magnetic resonance spectrum) occasional contamination (up to 10%) by phthalic anhydride. This impurity causes no subsequent difficulties. Washing of the crude reaction mixture with cold aqueous sodium hydrogen carbonate resulted in serious product loss because of its appreciable solubility in this medium and therefore should be avoided.

12. An earlier report of this sulfone cites a melting point of 39.5–41.0°.⁶

13. Available from Ventron Corp.

14. A 50-ml. syringe was employed and a series of transfers was therefore necessary.

15. The dioxane was dried before use by distillation from calcium hydride.

16. The apparatus consisted of a 5-l., three-necked, round-bottomed flask equipped also with a mechanical stirrer and reflux condenser capped with a nitrogen-inlet tube.

17. The addition rate is such that a gentle reflux is maintained

without the need of external heating. Considerable evolution of gas is witnessed.

18. Hydrogen gas is vigorously evolved and the solids ultimately undergo a color change from gray to white.

19. *Caution! Because of the presence of malodorous by-products, it is recommended that the extraction and distillation be conducted in a well-ventilated hood.*

20. The proton magnetic resonance spectrum (carbon tetrachloride) consists of a broad methine signal centered at δ 2.55 and a methyl singlet at δ 1.53 superimposed upon a methylene absorption at δ 1.25–1.85. Vapor phase chromatographic analysis denoted a purity of > 98%.

21. The checkers performed this step on one-half scale and obtained comparable results. However, when the product was distilled at higher pressures, b.p. 94–95° (ca. 70 mm.), consistently lower yields were obtained, in the range of 17–18%.

3. Discussion

1-Substituted and 1,2-disubstituted cyclobutenes have previously been prepared by irradiation of 1,3-butadienes capable of photocyclization,⁷⁻⁹ carbenic decomposition of acylcyclopropane tosylhydrazones,¹⁰ photocycloaddition of α,β -unsaturated ketones to alkynes,¹¹ and reductive ring expansion of cyclopropane 3-carboxylates.¹² However, these and yet other less known methods¹³⁻¹⁶ lack generality. The present procedure¹⁷ is a versatile scheme which is widely applicable in scope.¹⁸⁻²⁰ Since a variety of five-membered ring sulfones are readily available from a number of different precursors, the method is fully applicable to a broad spectrum of structural types. Its application to the preparation of mutually stable cyclooctatetraene bond shift isomers is noteworthy.²⁰ The present procedure is illustrative of the general method. Other examples are given in Table I.

Such reductive ring contractions of sulfones are formally similar to two other methods capable of supplanting a sulfur atom by a carbon-carbon double bond: the Ramberg-Bäcklund²¹ and Stevens rearrangements.²² The distinguishing feature of this novel approach to cyclobutenes consists in the resultant higher level of alkyl substitution at the sp^2 -hybridized centers.

TABLE I
REDUCTIVE RING CONTRACTION OF α,α' -DISUBSTITUTED
SULFOLANE ANIONS WITH LITHIUM ALUMINUM HYDRIDE

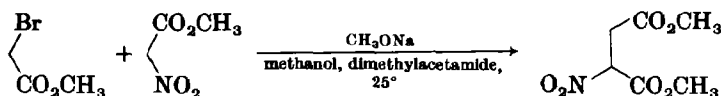
Sulfolane	Product	Overall yield, %
		54
		62
		67
		22
		20
		34

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DIMETHYL NITROSUCCINATE

[Butanedioic acid, 2-nitro-, dimethyl ester]



Submitted by S. ZEN and E. KAJI¹

Checked by M. BRAUN and G. BÜCHLI

1. Procedure

In a 1-l., three-necked, round-bottomed flask equipped with a calcium chloride drying tube, a mechanical stirrer, and a ground-glass stopper are placed 28.2 g. (0.184 mole) of freshly distilled methyl bromoacetate, 500 ml. of anhydrous *N,N*-dimethylacetamide (Note 1), and 20.0 g. (0.168 mole) of methyl nitroacetate (Note 2). The solution is stirred vigorously while 146 ml. (0.168 mole) of 1.15*N* sodium methoxide in

methanol is added in one portion. The resulting light-yellow suspension is stirred for an additional 16 hours at room temperature during which time it changes into a clear yellow solution.

After dilution with 200 ml. of benzene, the solution is transferred to a 2-l. separatory funnel containing 800 ml. of ice water and shaken thoroughly. The aqueous layer is separated, acidified to pH 3-4 with 2-3 ml. of concentrated hydrochloric acid, and extracted with three 100-ml. portions of benzene. All the organic layers are then combined and dried over anhydrous sodium sulfate. Filtration and concentration of the solution with a rotary evaporator, followed by exposure to high vacuum for 2-3 hours, affords 17.3-19.3 g. of the crude product (Note 3). Low-boiling impurities are removed by vacuum distillation (Note 4), the residual oil (14-15 g.) is transferred to a 50-ml. flask equipped with a short-path distillation apparatus, and vacuum distillation is continued. A forerun is taken until no rise in boiling point is observed, and then 7.2-8.5 g. (23-27%) of dimethyl nitrosuccinate is collected as a colorless oil, b.p. 85° (0.07 mm.), n^{20}_D 1.4441 (Note 5).

2. Notes

1. *N,N*-dimethylacetamide was treated with molecular sieves for 2 days, decanted, and distilled under reduced pressure, b.p. 85° (30 mm.), before use.

2. Methyl nitroacetate was prepared by the method of Zen and co-workers.² It should be distilled before use.

3. Gas chromatographic analysis of the crude mixture (SE-30 on Chromosorb W, 1 m., 150°) showed the presence of some low-boiling materials (including unreacted methyl nitroacetate) and a significant amount of the doubly alkylated by-product, trimethyl 2-nitro-1,2,3-propanetricarboxylate.

4. The bath temperature should be maintained below 70-75°. Distillation was carried out using a Claisen head, and the receiving flasks were immersed in ice.

The checkers found it convenient to omit this distillation and the subsequent transfer. Instead the crude product was placed in a 25-ml. flask and carefully distilled at 0.07 mm. The bath temperature was raised slowly, and a forerun was collected until the boiling point stabilized.

5. The distilled product was determined by the checkers to be 85-90% pure (gas chromatographic analysis), the major impurity being

the doubly alkylated by-product. Purity can be increased to 95% by redistillation. The checkers found that conducting the experiment on a $\frac{3}{4}$ scale resulted in increased yield (34%) and purity (90–93%) of once-distilled product.

For twice-distilled material: infrared (liquid film) cm^{-1} : 1745 strong, 1565 strong, 1430 medium strong; proton magnetic resonance (chloroform-*d*) (number of protons, multiplicity, coupling constant *J* in Hz): 3.14–3.45 (1, multiplet), 3.76 (3, singlet), 3.86 (3, singlet), 5.6 (1, doublet of doublets, *J* = 6 and 8).

3. Discussion

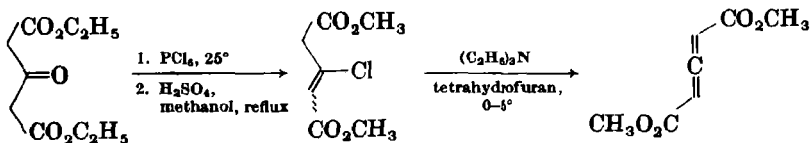
Diethyl nitrosuccinate has been prepared by oxidation of diethyl nitrososuccinate.³ It has also been synthesized by the reaction of sodium nitrite with diethyl bromosuccinate, but in this case no experimental conditions were described.⁴

The present method is a simple, one-step procedure employing commercially available or readily accessible starting materials. Other α -nitro carboxylic esters may be prepared in this way;⁵ for example, dimethyl 2-nitropentanedioate was prepared in 45–50% yield.

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DIMETHYL 2,3-PENTADIENEDIOATE

[2,3-Pentadienedioic acid, dimethyl ester]



Submitted by T. A. BRYSON and T. M. DOLAK¹
 Checked by R. SHAPIRO and G. BÜCHI

1. Procedure

Caution! The reaction of phosphorous pentachloride with diethyl acetone-1,3-dicarboxylate should be carried out in a hood, since hydrogen chloride is evolved.

A. *Dimethyl 3-Chloro-2-pentenedioate.* A dry 500-ml., three-necked, round-bottomed flask, fitted with a ground-glass stopper, a condenser provided with a gas bubbler, a gas-inlet adapter attached to a nitrogen (or argon) source, and a magnetic stirring bar, is charged with 60.0 g. (0.297 mole) of diethyl acetone-1,3-dicarboxylate [Pentanedioic acid 3-oxo-, diethyl ester] (Note 1). A steady, gentle flow of nitrogen is started through the reaction vessel (Note 2), and 65.0 g. (0.313 mole) of phosphorous pentachloride (Note 3) is added in thirteen approximately equal portions through the stoppered joint to the neat diester at 3-minute intervals with vigorous stirring (Note 4). After the addition is complete, the reaction mixture is warmed to 40° in a water bath for 30 minutes. The red solution is cooled in an ice bath and poured onto *ca.* 100 ml. of ice in a 500-ml. Erlenmeyer flask immersed in an ice bath. A 1:1 mixture of water and dichloromethane is used to rinse traces of the product from the reaction vessel into the Erlenmeyer flask, and the resulting mixture is stirred for 15 minutes (Note 5). After separating the two layers, the aqueous phase is extracted with three 100-ml. portions of dichloromethane and the combined organic extracts are dried over anhydrous sodium sulfate. Filtration through glass wool and removal of solvents with a rotary evaporator affords *ca.* 60 g. of a red oil. This is placed in a 500-ml., round-bottomed flask containing 20 ml. of concentrated sulfuric acid in 300 ml. of anhydrous methanol (Note 6), and the solution is refluxed using a heating mantle for 18 hours. Excess methanol (200 ml.) is distilled, and the residual yellow solution is cooled to room temperature and poured into 100 ml. of water. Sodium chloride is added to saturation, and the solution is extracted with eight 100-ml. portions of ether. The combined extracts are washed successively with 150 ml. of aqueous saturated sodium hydrogen carbonate and 150 ml. of aqueous saturated sodium chloride, then dried over anhydrous sodium sulfate. Filtration and concentration of the extract with a rotary evaporator affords a yellow oil which is distilled to yield 33.5–34.4 g. (59–60%) of dimethyl 3-chloro-2-pentadienedioate² as a colorless liquid, b.p. 50–60° (0.02 mm.) (Note 7).

B. *Dimethyl 2,3-Pentadienedioate.* In a 500-ml., three-necked, round-

bottomed flask, equipped with a gas-inlet adapter, a 50-ml. addition funnel, a ground-glass stopper, and a magnetic stirring bar, is placed 27.0 g. (0.14 mole) of the ester from Part A and 100 ml. of anhydrous tetrahydrofuran (freshly distilled from sodium) is added. The flask is flushed with nitrogen (or argon), and a positive pressure is maintained while the contents are cooled to 0° in an ice-salt bath and stirred with an efficient motor. Triethylamine (22 ml., 0.16 mole, freshly distilled from calcium hydride) is added through the addition funnel over a 10-minute period, the gas-inlet adapter is replaced with a calcium chloride tube, and the mixture is stirred at 0–5° for 18 hours (Note 8). The precipitate is removed by vacuum filtration and washed with three 100-ml. portions of anhydrous ether, and the combined filtrate and washings are washed successively with three 75-ml. portions of 0.1*N* hydrochloric acid and 100 ml. of aqueous saturated sodium chloride. After drying over anhydrous sodium sulfate, the ethereal solution is filtered, concentrated with a rotary evaporator, and the residual oil is distilled (Note 9) to yield 13.3–13.9 g. (61–64%) of dimethyl 2,3-pentadienedioate³ (Note 10), b.p. 58° (0.02 mm.).

2. Notes

1. Diethyl acetone-1,3-dicarboxylate was purchased from the Aldrich Chemical Company, Inc., and the checkers distilled this material under reduced pressure, b.p. 135–137° (12 mm.), discarding *ca.* 10% as a forerun.

2. A continuous flow of inert gas removes hydrogen chloride and phosphoryl chloride from the reaction flask.

3. The checkers used phosphorous pentachloride purchased from the J. T. Baker Chemical Company; the submitters used phosphorous pentachloride purchased from Eastman Organic Chemicals.

4. Warming and foaming occur during the addition and the temperature reaches *ca.* 40–45°.

5. The checkers found that unless the aqueous workup is cooled, the dichloromethane boils vigorously.

6. The checkers used commercial “anhydrous” methanol without further drying.

7. The checkers determined the product to be a mixture of isomers (approximately 6:1) by gas chromatographic analysis (15% SE-30 on Chromosorb W, 0.3 × 244 cm., 175°) and by proton magnetic resonance.

The mixture was characterized as follows: infrared (liquid film) cm.^{-1} : 1745 strong (shoulder at 1720), 1640 medium strong, 1440 medium strong; proton magnetic resonance (chloroform-*d*) δ (multiplicity, number of protons): 3.75 (singlet, 6), 4.12 (singlet, 2), 6.21 and 6.30 (two singlets, 1).

8. During this time a heavy precipitate of triethylamine hydrochloride forms; the mixture first becomes yellow and eventually brown in color.

9. The allene apparently polymerizes during distillation; it yellows in the receiving flask, and becomes orange and viscous even in the refrigerator overnight. The submitters obtained higher yields by distilling the product in batches.

10. The checkers further characterized the product as follows: infrared (liquid film) cm.^{-1} : 1970 strong, 1720 strong, 1440 strong; proton magnetic resonance (chloroform-*d*) δ (multiplicity, number of protons): 3.81 (singlet, 6), 6.10 (singlet, 2).

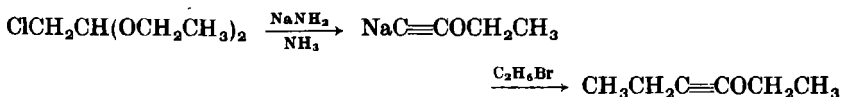
3. Discussion

Dimethyl 2,3-pentadienedioate has also been prepared from the enol phosphate of diethyl acetone-1,3-dicarboxylate.⁴

1. Department of Chemistry, University of South Carolina, Columbia, S.C. 29208.
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1-ETHOXY-1-BUTYNE

[1-Butyne, 1-ethoxy-]



Submitted by MELVIN S. NEWMAN¹ and W. M. STALICK²
 Checked by P. J. KOZIENSKI and G. BÜCHI

1. Procedure

A 1-l., three-necked, round-bottomed flask is equipped with an efficient dry-ice condenser (Note 1), a mechanical stirrer, and a gas-inlet tube. The flask is immersed in an acetone-dry ice bath and 600 ml. of anhydrous ammonia is introduced. After replacing the inlet tube with a

stopper, the cooling bath is lowered but kept beneath the flask. To the slowly stirred ammonia is added 0.5 g. of hydrated ferric nitrate. Air, dried by passing through calcium chloride, is bubbled through the solution for about 10 seconds (Note 2) after a small piece of freshly cut sodium is added (Note 3). Once hydrogen evolution has ceased, the blue color is discharged, leaving a finely divided black precipitate. Small pieces of freshly cut sodium are then added over a 20 minute period until 36.0 g. (1.56 g.-atom) has been added. After the formation of sodium amide is complete (Note 4), the stopper is replaced by a pressure-equalizing dropping funnel containing 76.1 g. (0.50 mole) of chloroacetaldehyde diethyl acetal [1-chloro-2,2-diethoxyethane] (Note 5) and the addition is made over a period of 20 minutes (Note 6). After 30–60 minutes the mixture has become light gray and 120 g. (1.10 mole) of freshly distilled ethyl bromide is added rapidly through the addition funnel (Note 7). The mixture is then stirred vigorously for 2.5 hours after which 30 ml. of cooled, saturated ammonium chloride solution is *cautiously* added through the addition funnel. This is followed by the addition of 120 ml. of pentane and an additional 370 ml. of the cooled, saturated ammonium chloride solution. The contents of the flask are transferred to a 2-l. separatory funnel (in the hood) and the lower aqueous layer removed and extracted with two 75-ml. portions of pentane (Note 8). The combined organic layers are filtered through glass wool to dissipate any emulsions, dried over magnesium sulfate, and filtered through a coarse-fritted funnel with gentle suction into a 500-ml., round-bottomed flask. A magnetic stirring bar is added and the pentane is removed by distillation at atmospheric pressure through a 20 × 2 cm. column packed with glass beads (Note 9) fitted with a well-cooled fractionating head. The yellow residue is distilled under reduced pressure (Note 10) with rapid magnetic stirring into dry ice-cooled receivers with an acetone–dry ice trap between the receiver and the vacuum source. The pure 1-ethoxy-1-butyne is collected as a clear, colorless liquid at 43–45° (50 mm.). A lower-boiling fraction collected at 20–42° (50 mm.) is combined with any material removed from the dry-ice trap and redistilled to yield additional product. Total yields of 30.2–32.3 g. (62–66%) are obtained (Note 11).

2. Notes

1. A gas bubbling device is attached to the dry-ice condenser. A simple apparatus consists of two 500-ml. filtering flasks equipped with

one-hole neoprene stoppers and glass tubing extending to the bottom of the flasks. The two flasks are connected through the glass tubing by a short piece of Tygon tubing. About 150 ml. of mineral oil is then placed in the flask distant from the condenser.

2. The checkers found that air was not necessary to initiate the formation of sodium amide. See Ref. 8.

3. The sodium is cut under dry pentane just before introducing each sample into the flask.

4. Complete conversion into sodium amide is indicated by cessation of gas evolution and disappearance of the blue color of the solution. This generally requires 20–30 minutes and results in a gray suspension of sodium amide in a dark-gray reaction medium.

5. Chloroacetaldehyde diethyl acetal was used as obtained from Aldrich Chemical Company, Inc.

6. During any of the additions in this preparation excessive foaming may occur. This may be effectively diminished by interrupting the addition of the reagent or by brief immersion of the reaction flask in the acetone–dry ice bath. If foaming has reached the condenser, be certain that the condenser is not plugged before proceeding.

7. The addition of ethyl bromide is accompanied by vigorous reflux of the ammonia and should be carefully monitored.

8. Since 1-ethoxy-1-butyne is very volatile, extreme care should be taken during the work-up to minimize loss of product due to evaporation. Extractions especially should be accompanied by careful and frequent venting of the separatory funnel to prevent excessive pressure.

9. The checkers used a 20-cm. Widmer column for the distillation.

10. The pot temperature should be kept below 80°. Distillation must be conducted at temperatures below 90° to preclude dimerization.³

11. Infrared (carbon tetrachloride) cm.^{-1} , strong peaks: 1245, 1230, 1015, 855. Proton magnetic resonance (carbon tetrachloride) δ (multiplicity, number of protons, assignment): 3.99 (quartet, 2, $-\text{OCH}_2-$), 2.13 (quartet, 2, $\text{C}\equiv\text{C}-\text{CH}_2-$, and 1.23 (overlapped triplets, 6, $2-\text{CH}_3$).

3. Discussion

The synthesis of 1-ethoxy-1-butyne has been reported previously, but the preparations have required multistep sequences. Two of the procedures use 1,2-dibromo-1-ethoxy butane which is dehydrohalogenated in two successive steps, first by an amine base and then by either powdered potassium hydroxide⁴ or sodium amide;⁵ no yields are given. The

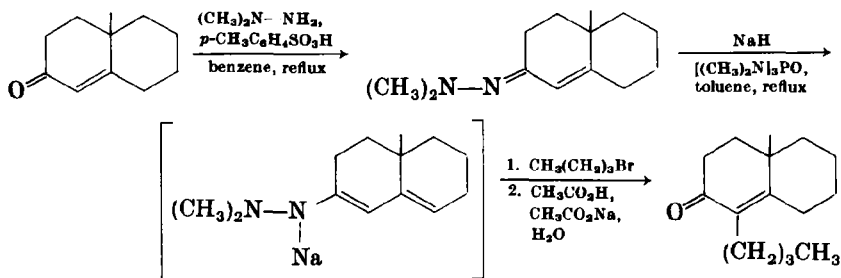
other procedure starts with 1,2-dibromoethyl ethyl ether which, upon treatment with *N,N*-diethylaniline, yields 2-bromovinyl ethyl ether. When 2-bromovinyl ethyl ether is allowed to react with lithium amide in ammonia and alkylation with diethyl sulfate follows, 1-ethoxy-1-butyne is isolated in about 55% yields.⁶

Some studies seeking preferred conditions for this reaction have been reported.⁷ Optimum yields of 1-ethoxy-1-propyne and 1-ethoxy-1-butyne are found when the product is worked up before allowing the ammonia solvent to evaporate, as the product evidently volatilizes with the ammonia. An experiment with 1-ethoxy-1-propyne showed a marked increase in yield when ammonia predried over calcium hydride was used instead of ammonia directly from the cylinder. A twofold excess of ethyl bromide is required to obtain a good yield of 1-ethoxy-1-butyne, since elimination apparently competes with alkylation in this case.

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**MONOALKYLATION OF α,β -UNSATURATED KETONES
via METALLOENAMINES:
1-BUTYL-10-METHYL- $\Delta^{1(9)}$ -2-OCTALONE**

[2(3*H*)-Naphthalenone, 1-butyl-4,4a,5,6,7,8-hexahydro-4a-methyl-]



Submitted by G. STORK¹ and J. BENAIM²

Checked by K. J. BRUZA, R. K. BOECKMAN, and C. R. JOHNSON

1. Procedure

*Caution! Hexamethylphosphoric triamide vapors have been reported to cause cancer in rats [J. A. Zapp, Jr., Science, **190**, 422 (1975)]. All operations with hexamethylphosphoric triamide should be performed in a good hood, and care should be taken to keep the liquid off the skin.*

A. 10-Methyl- $\Delta^{1(9)}$ -2-octalone N,N-Dimethylhydrazone. A 250-ml., round-bottomed flask equipped with a magnetic stirring bar and a Dean-Stark water separator is maintained under a dry nitrogen atmosphere (Note 1) and charged with 7.4 g. (0.045 mole) of 10-methyl- $\Delta^{1(9)}$ -2-octalone [2(3*H*)-Naphthalenone, 4,4a,5,6,7,8-hexahydro-4a-methyl-] (Note 2), 9.0 g. (0.15 mole) of *N,N*-dimethylhydrazine, 150 ml. of dry benzene, and 0.02 g. of *p*-toluenesulfonic acid. This mixture is refluxed for 10–14 hours, after which time no further water separates. Benzene and excess *N,N*-dimethylhydrazine are then removed by simple distillation, and the residue is distilled under reduced pressure to give 8.1 g. (87%) of the dimethylhydrazone as a pale-yellow liquid, b.p. 94–98° (0.2 mm.) (Notes 3, 4).

B. 1-Butyl-10-methyl- $\Delta^{1(9)}$ -2-octalone. A 250-ml., three-necked flask equipped with a magnetic stirring bar, a reflux condenser, a 50-ml., pressure-equalizing funnel, and a rubber septum is charged with 1.4 g. (0.032–0.035 mole) of 55–60% sodium hydride dispersion in mineral oil

and put under a dry nitrogen atmosphere. The mineral oil is then removed by washing the sodium hydride three or four times with 5-ml. portions of dry toluene (Note 5). A solution of 6.12 g. (0.030 mole) of 10-methyl- $\Delta^{1(9)}$ -2-octalone *N,N*-dimethylhydrazone in 100 ml. of dry toluene is placed in the flask and 10 ml. of dry hexamethylphosphoramide is added. The rubber septum is replaced with a glass stopper. The solution is warmed with an oil bath to reflux the toluene; hydrogen evolution is observed. Reflux is maintained for 14–16 hours, during this time the solution becomes dark brown. The solution is then cooled to -10° and 4.5 g. (0.033 mole) of 1-bromobutane in 10 ml. of dry toluene is slowly added. The solution is warmed to 60° and maintained at that temperature for 4–5 hours. An abundant precipitate of sodium bromide is formed. The solution is cooled to 0° and an acetate-buffer solution (Note 6) is added. The mixture is refluxed for 4–5 hours to complete the hydrolysis. It is then cooled and decanted. The aqueous phase is extracted three times with 25-ml. portions of ethyl ether. The combined organic layers are successively washed three times with 80- to 100-ml. portions of 10% hydrochloric acid, three times with 50-ml. portions of a saturated sodium hydrogen carbonate solution, twice with 50-ml. portions of a saturated sodium chloride solution, and then dried over sodium sulfate. The solvents are removed by rotary evaporation (Note 7). The residue is distilled under high vacuum using a short column. After a small forerun, 4.3–4.7 g. (65–72%) of pure 1-butyl-10-methyl- $\Delta^{1(9)}$ -2-octalone, b.p. $84\text{--}92^{\circ}$ (0.2 mm.), is obtained (Note 8).

2. Notes

1. A positive pressure of nitrogen is maintained using a mercury bubbler.

2. The 10-methyl- $\Delta^{1(9)}$ -2-octalone, which can be prepared from 4-(diethylamino)-2-butanone, 2-methylcyclohexanone, and sodium,³ has b.p. $65\text{--}70^{\circ}$ (0.1 mm.) and n_D^{20} 1.523. Infrared (neat) cm.^{-1} : 1610, 1670; proton magnetic resonance (carbon tetrachloride) δ (assignment): 5.6 (vinyl CH), 1.25 (angular CH_3).

3. The hydrazone should be stored under dry nitrogen at -10° .

4. Proton magnetic resonance (carbon tetrachloride) δ (multiplicity, assignment): 6.35 (40%) and 5.70 (60%) (singlets, vinyl hydrogens of diastereomeric hydrazones), 2.35 (singlet, $\text{N}(\text{CH}_3)_2$), 1.15 (singlet, C—CH_3); infrared (neat) cm.^{-1} : 1620, 1580; n_D^{20} 1.505.

5. A 5-ml. portion of dry toluene is introduced into the flask with a syringe, and sodium hydride dispersion is stirred for 1 minute. Then 4 ml. of the supernatant toluene is carefully removed from the flask with a syringe.

6. The buffer solution is prepared by dissolving 20 g. of anhydrous sodium acetate in a mixture of 40 ml. of acetic acid and 40 ml. of water.

7. At this point the submitters reported 7.07 g. of crude product which by gas chromatographic analysis on an SE 30 column at 200° showed 1-3% of 10-methyl- $\Delta^{1(9)}$ -2-octalone and 85% of the desired alkylated product.

8. Proton magnetic resonance (carbon tetrachloride) δ (multiplicity, assignment): 1.2 (singlet, angular CH_3); 0.9 (triplet, CH_3); infrared (neat) cm^{-1} : 1660, 1600; $n_D^{25} = 1.511$.

3. Discussion

Alkylations of enamines of α,β -unsaturated ketones with alkyl halides often give very poor yields of *C*-alkylated products because of competing *N*-alkylation.^{4,5} In the type of transformation illustrated here, direct alkylations of enamines are completely unsuccessful, even in cases where hindered enamines⁶ are used. On the other hand, the metallocenamine method⁷ can be applied generally with good success in the problem of monoalkylation of α,β -unsaturated ketones.⁸

Metallocenamines can be formed from *N,N*-dimethylhydrazones, as illustrated here, or from *N*-cyclohexylimines. Various strong bases have been used, including butyllithium, lithium diisopropylamide, sodium hydride, and lithium bis(trimethylsilyl)amide. The nature and sometimes the stoichiometry of the strong base used can be important. Poor yields of alkylated compounds are obtained with Grignard reagents, and in the case of butyllithium, excess base can result in the formation of significant amounts of kinetically controlled alkylation products (e.g., alkylation at C-3 of 10-methyl- $\Delta^{1(9)}$ -2-octalone). In the cases of octalones and steroid compounds (cholestenone, testosterone benzoate) it has been found that sodium hydride and lithium diisopropylamide gave the best yields of the desired alkylated compounds.⁸

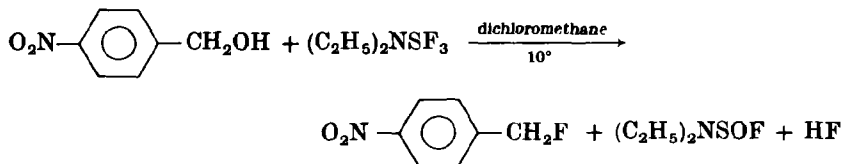
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***p*-NITROBENZYL FLUORIDE**

[Benzene, 1-(fluoromethyl)-4-nitro-]



Submitted by W. J. MIDDLETON and E. M. BINGHAM¹
 Checked by EUGENE R. KENNEDY, RONALD F. SIELOFF,
 and CARL R. JOHNSON

1. Procedure

Caution! Protective gloves should be worn when handling diethylaminosulfur trifluoride because this material can cause severe HF burns.

A dry 1-l., three-necked, round-bottomed flask is fitted with a 500-ml. dropping funnel, thermometer, a magnetic stirrer, and a reflux condenser protected from the atmosphere by a drying tube. The apparatus is flushed with dry nitrogen and 150 ml. of dry dichloromethane and 21 ml. (0.16 mole) of diethylaminosulfur trifluoride² are added to the flask. The contents of the flask are cooled to 10° and a solution of 23.0 g. (0.15 mole) of *p*-nitrobenzyl alcohol [Benzenemethanol, 4-nitro] (Note 1) in 450 ml. of dichloromethane is added dropwise at a fast rate (45 minutes). The reaction mixture is allowed to come to room temperature and then poured into a beaker containing 300 g. of ice to decompose any unreacted diethylaminosulfur trifluoride. The organic layer is separated and the water layer is extracted twice with 45-ml. portions of dichloromethane. The organic layer and extracts are combined, washed with 150 ml. of water, and dried over anhydrous magnesium sulfate.

Evaporation to dryness under reduced pressure gives 20.9–22.1 g. (90–95%) of crude product. Purification by recrystallization from 500 ml. of pentane yields 15.5 g. (67%) of *p*-nitrobenzyl fluoride as colorless needle-shaped crystals, m.p. 36–37° (Note 2).

2. Notes

1. *p*-Nitrobenzyl alcohol is available from Eastman Organic Chemicals or Aldrich Chemical Company, Inc.

2. An additional quantity of product of lesser purity can be obtained as a second crop by evaporation of the pentane.

3. Discussion

This procedure is an example of a broadly applicable, simple method for replacing the hydroxyl group of functionally substituted and unsubstituted primary, secondary, and tertiary alcohols with fluorine. Diethylaminosulfur trifluoride,² the fluorinating reagent used in this procedure, is less likely to cause rearrangements or dehydration than other reagents sometimes used for this purpose (SF₄, HF, HF·pyridine, SeF₄·pyridine, and (C₂H₅)₂NCF₂CHClF).³ Furthermore, diethylaminosulfur trifluoride is a liquid that can be measured easily and used in standard glass equipment at moderate temperatures and atmospheric pressure.

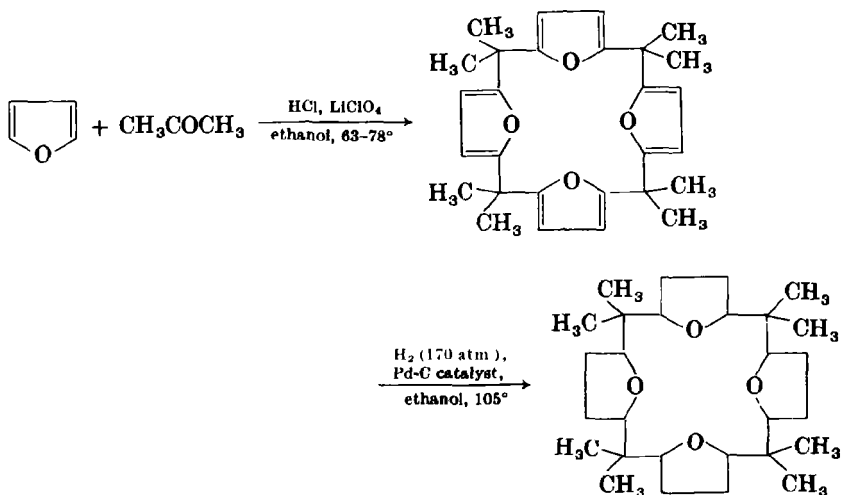
Some alcohols that have been converted into the corresponding fluorides by reactions with diethylaminosulfur trifluoride include 1-octanol, 2-methyl-2-butanol, isobutyl alcohol, cyclooctanol, ethylene glycol, crotyl alcohol, 2-phenylethanol, 2-bromoethanol, ethyl lactate, and ethyl α -hydroxynaphthaleneacetate.³

p-Nitrobenzyl fluoride has also been prepared in 40–60% yield by the reaction of *p*-nitrobenzyl bromide with mercuric fluoride⁴ and in mixture with the *ortho* and *meta* isomers by the nitration of benzyl fluoride.⁵

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2,2,7,7,12,12,17,17-OCTAMETHYL-21,22,23,24-TETRAOXAPERHYDROQUATERENE

[21, 22, 23, 24-Tetraoxapentacyclo-[16.2.1.1^{3,6}.1^{8,11}.1^{13,16}]tetracosane, 2,2,7,7,12,12,17,17-octamethyl-]



Submitted by MAURICE CHASTRETTE, FRANCINE CHASTRETTE,
and JEAN SABADIE¹

Checked by WILLIAM V. PHILLIPS, HERBERT O. HOUSE, JAMES C. KAUFER,
and WILLIAM A. SHEPPARD

1. Procedure

A. 2,2,7,7,12,12,17,17-Octamethyl-21,22,23,24-tetraoxaquaterene [21, 22, 23, 24-Tetraoxapentacyclo[16.2.1.1^{3,6}.1^{8,11}.1^{13,16}]tetracosane-3,5,8,10,13, 15,18,20-octaene, 2,2,7,7,12,12,17,17-octamethyl-]. In a 1-l., three-necked flask fitted with a mechanical stirrer, a dropping funnel, and a condenser are placed 27.2 g. (0.40 mole) of freshly distilled furan (Note 1), 24 ml. of absolute ethanol, 57.3 g. (0.20 mole) of the lithium perchlorate-1,2-dimethoxyethane complex (Note 2), and 16 ml. of reagent-grade concentrated hydrochloric acid. The resulting pale-yellow to pale-tan solution is stirred continuously and heated to 63° with an oil bath. Then to the hot, stirred solution 58.1 g. (0.80 mole) of acetone (Note 3) is added dropwise during 1 hour. During this addition

the heat of reaction causes the solution to reflux and some white solid begins to separate. After the addition is complete, stirring and heating are continued until refluxing ceases (about 30 minutes). Then the temperature of the bath is raised to 78° and the mixture is refluxed with stirring for an additional 30 minutes. The reaction mixture, a dark red-brown solution containing a pasty white precipitate, is cooled to room temperature with continuous stirring and 25 ml. of water and 300 ml. of diethyl ether are added. The resulting mixture is stirred at room temperature for 1 hour to convert the precipitate into a finely divided white solid, and then the mixture is filtered with suction employing a medium-porosity, sintered-glass funnel. The residual crude product is washed thoroughly (Note 4) with portions of diethyl ether (total volume 100 ml.) followed by portions of 95% ethanol (total volume 50 ml.), and then the crude solid product (14.2–14.8 g.) is allowed to dry in the air. The crude product, m.p. 231–240° is recrystallized from 140–150 ml. of reagent-grade chloroform to yield an initial crop of product as white needles, 7.3–7.4 g., m.p. 241.5–243°. The mother liquors are concentrated to one-third their initial volume to separate a second crop of crystalline product, 2.9–3.1 g., m.p. 240–242°. The total yield of the tetraoxaquerene is 10.2–10.5 g. (24–25%) (Note 5).

B. 2,2,7,7,12,12,17,17-Octamethyl-21,22,23,24-tetraoxaperhydroquaterene. A 400-ml., stainless-steel shaking autoclave is charged with 4.0 g. (0.0092 mole) of the tetraoxaquerene from Part A, 200 ml. of ethanol, and 400 mg. of 5% palladium on charcoal catalyst (Note 6). The autoclave is filled with hydrogen at an initial pressure of 170 atm. and heated with shaking for 4 hours at 105°. Catalyst and a white solid are removed by filtration (Note 7), the solid is dissolved in 100 ml. of warm chloroform, the solution is filtered, the chloroform is evaporated, and the white solid which is obtained is dried under reduced pressure at 60° (Note 8). The tetraoxaperhydroquaterene is obtained as a white solid, m.p. 204–209° (Note 9), in a yield of 2.85–2.97 g. (69–72%).

2. Notes

1. Furan, purchased from Aldrich Chemical Company, Inc., was distilled before use; b.p. 31–32°.

2. Anhydrous lithium perchlorate (60 g.) obtained from Ventron Corporation was placed in a 500-ml. flask under dry nitrogen, and 85 ml. of anhydrous 1,2-dimethoxyethane was added. The mixture became

warm. The resulting mixture was swirled and finally heated on the steam bath under dry nitrogen until all of the solid dissolved. The resulting solution was cooled and gradually crystallized to a solid mass. Additional 1,2-dimethoxyethane (155 ml.) was added, the mixture was stirred, and supernatant liquid was removed with a sintered-glass filter stick. The resulting solid was vacuum dried briefly in a vacuum dessicator which was pumped to 0.3 mm. for 20 minutes, then sealed under vacuum overnight. The resulting solvated lithium perchlorate, $\text{LiClO}_4(\text{C}_4\text{H}_{10}\text{O}_2)_2$, weighed 108 g. It may be stored in a brown bottle under dry nitrogen until needed.

When the lithium perchlorate was dissolved initially in the entire 240 ml. of 1,2-dimethoxyethane and processed as above, the yield was considerably lower. The submitters report that, if less lithium perchlorate is used in the preparation of the octamethyltetraoxaquerene, the yield of the product is lowered.

3. Reagent-grade acetone was used. The submitters state that an excess of acetone is necessary. When a 1:1 mole ratio of acetone to furan was used, they obtained only a 21% yield of crude product, and when a 1:2 ratio of acetone to furan was employed, the yield of product was less than 5%.

4. The submitters report that, if this material is not washed thoroughly to remove the soluble linear polymers of low molecular weight present, the crude product will melt and/or darken at much lower temperatures than 231–240°.

5. The product has the following spectral properties; nuclear magnetic resonance (chloroform-*d*) δ (multiplicity, number of protons, assignment): 5.90 (singlet, 8, aryl CH), 1.48 (singlet, 24, CH_3); mass spectrum *m/e* (relative intensity): 432 (M^+ , 40) 418 (34), 417 (100), 201 (28), 186 (31), 149 (55), 85 (46), 83 (67), 75 (21), 60 (21), 47 (20), 45 (24), 43 (53), and 41 (26).

6. Catalyst obtained from Engelhard Industries was used. The submitters used 200 mg. of Fluka 10% palladium on charcoal catalyst with 5 g. of starting material in 250 ml. of ethanol and obtained a total yield of 2.3 g. (46%), m.p. 208–211°.

7. The ethanolic filtrate can be concentrated to 10–15 ml. under reduced pressure to obtain 0.3 g. (7%) of crude product, m.p. 187–202°. Unchanged starting material, if present, is concentrated in this second fraction and may be detected by the furan resonance at δ 5.85 in the proton magnetic resonance spectrum or by a sharp infrared absorption

at 772 cm.^{-1} which is not present in the product. Elemental analyses of these second crops suggested that other impurities were also present.

8. The solid tenaciously holds a small amount of chloroform which can be detected by proton magnetic resonance (δ 7.25). Vacuum drying overnight at 60° removes this impurity.

9. In one isolated case the checkers found that no hydrogen uptake occurred, and unreacted starting material was recovered. This erratic result may have resulted from accidental poisoning of the catalyst by contaminants present in the apparatus or associated valves and lines. If multiple runs are carried out, the products of each should be checked by infrared or proton magnetic resonance spectroscopy before being combined. The spectral properties of the product are: proton magnetic resonance (chloroform-*d*) δ (multiplicity, number of protons, assignment): 0.74, 0.82, 0.93, 1.04 (singlets, 24, CH_3); 1.2–1.9 (multiplet, 16 CH_2), 1.9–2.8 (multiplet, 4, CH_2), and 3.0–4.2 (multiplet, 8, CH); infrared (Nujol) cm.^{-1} strong absorptions: 1078, 1039, medium: 999, 991, 552, 528, 520, and weaker: 1285, 1248, 1204, 977, 884, 840, 659, 719, 598, 560. The checkers concluded from examination of properties that a variable mixture of isomers is obtained from the hydrogenation.

3. Discussion

The unsaturated tetraoxaquaterene (accompanied by linear condensation products) was first synthesized in 18.5% yield by the acid-catalyzed condensation of furan with acetone in the absence of added lithium salts.² Other ketones also condensed with furan to give analogous products in 6–12% yield.^{2–4} A corresponding macrocycle was also prepared in 9% yield from pyrrole and cyclohexanone.⁴ The macrocyclic ether products have also been obtained by condensation of short linear condensation products having 2, 3, or 4 furan rings with a carbonyl compound.⁵

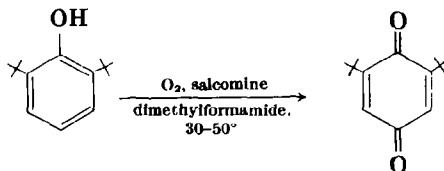
The method described here gives higher yields of the macrocyclic tetraethers and allows the product from furan and cyclohexanone to be formed directly in 5–10% yield, whereas this product was previously obtained only by an indirect route. The added lithium perchlorate undoubtedly accelerates the reaction, since after short reaction times the product was isolated in 20% yield when the salt was present and in only 5% yield when the salt was absent. The lithium cation is presumably acting as a template which coordinates with the oxygen atoms of

the furan units to favor cyclization instead of linear polymerization.⁶ The hydrogenated macrocycle has been shown to form complexes with lithium salts.^{6,7}

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OXIDATION WITH BIS(SALICYCLIDENE)ETHYLENEDIIMINO-COBALT(II) (SALCOMINE): 2,6-DI-*tert*-BUTYL-*p*-BENZOQUINONE

[2,5-Cyclohexadiene-1,4-dione, 2,6-di-*tert*-butyl-]



Submitted by C. R. H. I. DE JONGE, H. J. HAGEMAN,
G. HOENTJEN and W. J. MIJS¹

Checked by K. BALASUBRAMANIAN, ROBERT K. BOECKMAN,
and CARL R. JOHNSON

1. Procedure

In a 200-ml., three-necked flask equipped with a mechanical stirrer, a thermometer, and a gas-inlet tube are placed 41.2 g. (0.2 mole) of 2,6-di-*tert*-butylphenol (Note 1) in 75 ml. of dimethylformamide (Note 2) and 2.5 g. (0.0075 mole) of salcomine (Note 3). With stirring, oxygen is introduced at such a rate that the temperature does not exceed 50°. This is continued for 4 hours. At the end of the reaction the temperature drops to about 25°. The reaction mixture is then poured onto 500 g. of crushed ice and 15 ml. of 4*N* hydrochloric acid. A yellow-brown precipitate is formed. The solid material is collected by suction filtration and washed on the filter three times with 50-ml. portions of 1*N* hydrochloric

acid, three times with 100-ml. portions of water, and twice with 25-ml. portions of cold ethanol. Drying under reduced pressure at 50° for 3 hours gives 43 g. of crude 2,6-di-*tert*-butyl *p*-benzoquinone as a dark-yellow crystalline solid. Recrystallization from ethanol gives 36.5 g. (83%) of pure 2,6-di-*tert*-butyl-*p*-benzoquinone, m.p. 65–66° (Notes, 4, 5).

2. Notes

1. 2,6-Di-*tert*-butylphenol purchased from Aldrich Chemical Company, Inc., was used.

2. When chloroform or methanol is used as the solvent for the oxidation of phenols, other products, originating from coupling of aryloxy radicals, *e.g.*, polyphenylene ethers and/or diphenoquinones, are also formed.²

3. Bis(salicylidene)ethylenediiminocobalt (II) can be prepared according to the procedure described by H. Diehl and C. C. Hack, *Inorg. Syn.*, **3**, 196 (1950).

4. 2,6-Di-*tert*-butyl-*p*-benzoquinone should be stored in a brown bottle.

5. The product has the following spectral properties; infrared (chloroform) cm^{-1} : 1652, 1597; proton magnetic resonance (chloroform-*d*) δ 1.33, 6.56.

3. Discussion

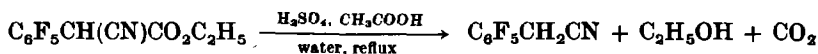
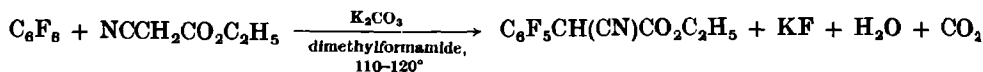
Various 2,6-disubstituted *p*-benzoquinones have been prepared by oxidation of the corresponding 2,6-disubstituted phenols with potassium nitrosodisulfonate^{3,4} or lead dioxide in formic acid.⁵ Oxidative coupling of 2,6-disubstituted phenols to poly-2,6-disubstituted phenylene ethers followed by treatment of the polymers in acetic acid with lead dioxide is reported⁶ to give low yields of the corresponding 2,6-disubstituted *p*-benzoquinones.

Salcomine is a useful catalyst for the selective oxygenation of 2,6-disubstituted phenols to the corresponding *p*-benzoquinones when dimethylformamide is used as the solvent; laborious procedures are avoided and high yields of pure *p*-benzoquinones are obtained. Following the procedure described above, the authors have prepared 2,6-diphenyl-*p*-benzoquinone (m.p. 134–135°, yield 86%) and 2,6-dimethoxy-*p*-benzoquinone (m.p. 252°, yield 91%) from the appropriate phenols.

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(PENTAFLUOROPHENYL)ACETONITRILE

[Benzeneacetoneitrile, 2,3,4,5,6-pentafluoro-]



Submitted by ROBERT FILLER¹ and SARAH M. WOODS²

Checked by ANDREW E. FEIRING and WILLIAM A. SHEPPARD

1. Procedure

A. *Ethyl Cyano(pentafluorophenyl)acetate*. A 2-l., four-necked flask equipped with mechanical stirrer, addition funnel, thermometer, and condenser is charged with 650 ml. of dimethylformamide (Note 1) and 140 g. (1.0 mole) of anhydrous potassium carbonate. The rapidly stirred mixture is heated to 152–154° and 113 g. (1.0 mole) of ethyl cyanoacetate is added dropwise during 10–15 minutes without further heating. The temperature of the mixture is allowed to drop to 110–120° and maintained within this range while 186 g. (1.0 mole) of hexafluorobenzene (Note 2) is added dropwise over 1 hour. The dark mixture is stirred for 3 hours after the addition is complete, then poured into 3 l. of ice water contained in a 5-l. Erlenmeyer flask, and acidified (*Caution! Foaming*) with 20% sulfuric acid. After cooling overnight in the refrigerator, the top aqueous layer is decanted from a lower, viscous organic layer. The organic layer is dissolved in 600 ml. of ether, washed with water, and 10% aqueous sodium hydrogen carbonate, and dried over anhydrous magnesium sulfate. The ether is removed on a rotary evaporator to afford 217 g. (78%) of dark oil which crystallizes on standing (Note 3). An analytical sample is prepared by dissolving 2 g.

of the crude material in 5 ml. of boiling 95% ethanol. Hexane is added until the mixture becomes turbid. Crystallization occurs when the mixture is cooled with vigorous stirring in an acetone-dry ice bath. The solid is quickly collected on a Büchner funnel and transferred to a sublimator. Sublimation at 30° (0.5–1.0 mm.) affords white crystals, m.p. 38–38.5°, of analytically pure ethyl cyano(pentafluorophenyl)acetate (Note 4).

B. (*Pentafluorophenyl*)acetoneitrile. A 1-l., one-necked flask equipped with magnetic stirrer and a reflux condenser is charged with 139.5 g. (0.5 mole) of crude ethyl cyano(pentafluorophenyl)acetate, 350 ml. of 50% aqueous acetic acid, and 12.5 ml. of concentrated sulfuric acid. The mixture is heated at reflux for 15 hours. After cooling to room temperature, the mixture is diluted with an equal volume of water and cooled in an ice bath for 1 hour. The top layer is decanted from a dark organic layer which settles to the bottom of the flask. The organic phase is dissolved in 200 ml. of ether and washed with water and 10% aqueous sodium hydrogen carbonate. After drying over anhydrous magnesium sulfate, the ether is removed on a rotary evaporator. The residue is distilled through a 25-cm. jacketed Vigreux column to afford 74–78 g. (71–75%) of (pentafluorophenyl)acetoneitrile as a colorless liquid, b.p. 105 (8 mm.), n^{25}_D 1.4370 (Note 5).

2. Notes

1. Technical-grade dimethylformamide is stirred over anhydrous cupric sulfate, filtered, and distilled under reduced pressure. The submitters used reagent-grade dimethylformamide without purification.

2. Hexafluorobenzene was purchased from PCR, Inc., Gainesville, Fl., and distilled (b.p. 80–81°) before use.

3. In one run the checkers obtained only 135 g. of crude product by this procedure. The aqueous solution which was decanted from the crude product was divided into three portions and each portion was extracted with one 250-ml. portion of ether. The combined ether extracts were washed with water and 10% aqueous sodium hydrogen carbonate, dried over anhydrous magnesium sulfate, and concentrated on the rotary evaporator to afford an additional 83 g. of crude product, for a total of 218 g.

4. Proton magnetic resonance (carbon tetrachloride) δ (multiplicity, number of protons): 1.38 (triplet, 3) 4.35 (quartet, 2), 5.05 (singlet, 1); infrared (chloroform) cm.^{-1} : 3003, 2933, 2257, 1760, 1661, 1527, 1513;

fluorine magnetic resonance (carbon tetrachloride) p.p.m. (CFCl_3 internal standard): 141.2 (symmetrical multiplet, 2 ortho F), 151.8 (triplet of triplets, 1 para F, $J_{12} = 20.3$ Hz, $J_{13} = 2.5$ Hz), 161.1 (multiplet, 2 meta F).

5. Proton magnetic resonance (carbon tetrachloride) δ : 3.75 (singlet with fine structure); infrared (neat) cm^{-1} : 2985, 2273, 1667, 1527, 1515; fluorine magnetic resonance (carbon tetrachloride) p.p.m. (CFCl_3 internal standard) 142.4 (symmetrical multiplet, 2 ortho F), 153.8 (triplet with fine structure, 1 para F, $J = 20$ Hz), 161.7 (multiplet, 2 meta F).

3. Discussion

The formation of ethyl cyano(pentafluorophenyl)acetate illustrates the *intermolecular* nucleophilic displacement of fluoride ion from an aromatic ring by a stabilized carbanion. The reaction proceeds readily as a result of the activation imparted by the electron-withdrawing fluorine atoms.³ The selective hydrolysis of a cyano ester to a nitrile has been described.⁴ (Pentafluorophenyl)acetonitrile⁵ has also been prepared by cyanide displacement on (pentafluorophenyl)methyl halides. However, this direct displacement is always accompanied by an undesirable side reaction to yield 15–20% of 2,3-bis(pentafluorophenyl)propionitrile.

(Pentafluorophenyl)acetonitrile is a useful intermediate to 4,5,6,7-tetrafluorindole.⁶ The nitrile is readily converted into 2-(pentafluorophenyl)ethylamine hydrochloride in 80% yield by catalytic hydrogenation in dilute hydrochloric acid. Although the salt is stable, the amine undergoes a facile intermolecular nucleophilic aromatic substitution reaction, even at room temperature. However, freshly distilled 2-(pentafluorophenyl)ethylamine is converted by heating in the presence of anhydrous potassium fluoride in dimethylformamide into 4,5,6,7-tetrafluorindoline (62% yield) by intramolecular nucleophilic displacement of fluoride ion.⁷ The indoline is aromatized by treatment with activated manganese dioxide⁸ to give 4,5,6,7-tetrafluorindole (82% yield).

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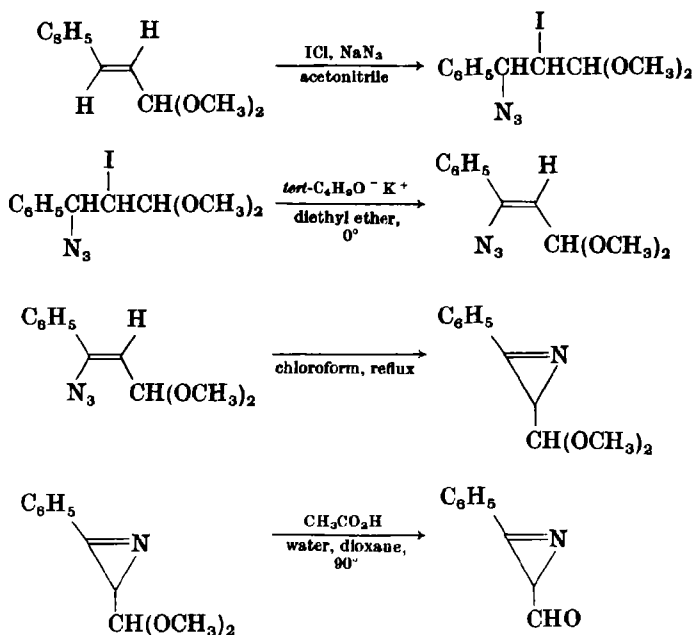
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3-PHENYL-2H-AZIRINE-2-CARBOXALDEHYDE

[2H-Azirine-2-carboxaldehyde, 3-phenyl-]



Submitted by ALBERT PADWA,¹ THOMAS BLACKLOCK,
and ALAN TREMPER

Checked by W. F. OETTLER, E. R. HOLLEB,
and WILLIAM A. SHEPPARD

1. Procedure

Caution! Although the organic azide intermediates used in this procedure have not shown any explosive hazard under the experimental conditions,

they should always be handled with adequate shielding and normal protective equipment such as face shield and leather gloves.

A. (1-Azido-2-iodo-3,3-dimethoxypropyl)benzene. A dry 1-l., three-necked, round-bottomed flask fitted with an efficient magnetic stirrer and two 250-ml. pressure-equalizing dropping funnels is charged with 75 g. (1.14 moles) of sodium azide and 450 ml. of dry acetonitrile (Note 1). The mixture is stirred and cooled in an ice-salt bath (-5° to 0°), and 83 g. (0.51 mole) of iodine monochloride (Note 2) is added dropwise from one of the addition funnels during 10–20 minutes. The solution is stirred for an additional 5–10 minutes and then 81 g. (0.45 mole) of cinnamaldehyde dimethylacetal [Benzene,(3,3-dimethoxy-1-propenyl)-] (Note 3) is added from the other dropping funnel over a 15–20 minute period while the cooling bath temperature is maintained at $0-5^{\circ}$. The resulting red-brown mixture is stirred for 12 hours at room temperature, poured into 500 ml. of water, and extracted with three 500-ml. portions of ether. The combined organic extracts are washed successively with 700 ml. of 5% aqueous sodium thiosulfate (Note 4) and 1 l. of water. The ether solution is dried over magnesium sulfate. The solvent is removed with a rotary evaporator to give the azide product as a residual orange oil (Note 5), 150–156 g. (97–98%), of sufficient purity to be used for the next step.

B. (1-Azido-3,3-dimethoxy-1-propenyl)benzene. In a 2-l., one-necked, round-bottomed flask equipped with a magnetic stirrer and powder funnel are placed 156 g. (0.45 mole) of the iodoazide from Part A and 1500 ml. of anhydrous ether. The solution is stirred and cooled in an ice-salt bath (-5° to 0°), and 62 g. (0.55 mole) of potassium *t*-butoxide (Note 6) is added. The powder funnel is then replaced by a calcium chloride drying tube and the mixture is stirred for 4–5 hours at 0° . At the end of this time 350 ml. of water is added while the mixture is still cold. The ethereal layer is then separated and washed with three 350-ml. portions of water and dried over magnesium sulfate. The solvent is removed with a rotary evaporator without heating, leaving 67–75 g. (68–76%) of (1-azido-3,3-dimethoxy-1-propenyl)-benzene as a dark oily liquid (Note 7). This material can be used without further purification for Part C (Note 8).

C. 2-(Dimethoxymethyl)-3-phenyl-2H-azirine. The crude product (71–75 g., 0.32–0.34 mole) obtained from Part B is heated at reflux in 1 l. of chloroform in a 2-l., round-bottomed flask for 12 hours (Note 9). The solvent is removed with a rotary evaporator and the crude residue

is distilled to give 48–61 g. (78–93%) of 2-(dimethoxymethyl)-3-phenyl-2H-azirine, b.p. 103–105° (0.27 mm.) as a colorless oil (Note 10).

D. 3-Phenyl-2H-azirine-2-carboxaldehyde. The product from Part C (59.0 g., 0.31 mole) is placed in a 3-l., three-necked, round-bottomed flask fitted with a mechanical stirrer, a reflux condenser, and a thermometer of sufficient length to extend into the liquid contents of the flask. After addition of 600 ml. of 1,4-dioxane (Note 11) and 800 ml. of 20% acetic acid, the mixture is stirred and heated sufficiently to bring the temperature of the reaction mixture up to 90° over a period of one hour (Note 12). The temperature of the reaction mixture is held at 90° for an additional 5 minutes, and then the flask is rapidly cooled in an ice-salt bath (–5° to 0°). The product is extracted with four 1-l. portions of ether, and the combined organic extracts are washed successively with 1 l. of aqueous 5% sodium hydrogen carbonate and 1-l. of saturated aqueous sodium chloride. After the ether layer has been dried over anhydrous magnesium sulfate, the solvent is removed with a rotary evaporator, and a mixture of 5 ml. of ether and 10 ml. of pentane is added. The residual oil is allowed to stand in a refrigerator (0–3°) for 12 hours to complete the crystallization of the crude product. The crystalline solid is collected on a cold filter and is sublimed at 35° (0.01 mm.) to give 13.3 g. (30%) (Note 13) of 3-phenyl-2H-azirine-2-carboxaldehyde, m.p. 49–51° (Note 14).

2. Notes

1. Reagent-grade acetonitrile (J. T. Baker Chemical Company) was used without further purification.

2. Iodine monochloride, purchased from J. T. Baker Chemical Company, was used without further purification.

3. Cinnamaldehyde dimethylacetal is prepared by the method used to prepare the corresponding diethylacetal.² A mixture of 66.0 g. (0.5 mole) of *trans*-cinnamaldehyde (Aldrich Chemical Company, Inc.), 100 g. (1.06 mole) of trimethyl orthoformate (Eastman Organic Chemicals), 450 ml. of anhydrous methanol (J. T. Baker Chemical Company), and 0.5 g. of *p*-toluenesulfonic acid monohydrate (Fisher Scientific Company) is stirred at room temperature for 24 hours. At the end of this time the alcohol is removed with a rotary evaporator and the residue is distilled to give 81–83 g. (91–93%) of cinnamaldehyde dimethylacetal, b.p. 93–96° (0.2 mm.).

4. The orange color of the ethereal solution is completely discharged after washing with 5% aqueous sodium thiosulfate.

5. The product has the following spectral properties: infrared (neat) cm.^{-1} : 2120 (strong N_3 absorption); proton magnetic resonance (chloroform- d), δ (multiplicity, number of protons, assignment, coupling constant J in Hz.): 3.38 (singlet, 3, OCH_3), 3.46 (singlet, 3, OCH_3), 3.93 (doublet, 1, 1 or 3 CH , $J = 4$), 4.38 (doublet of doublets, 1, CH , $J = 9$ and 4), 4.78 (doublet, 1, 1 or 3, CH , $J = 9$), 7.33 (singlet, 5, aromatic H).

6. Potassium *t*-butoxide, purchased from Columbia Organic Chemicals Company, Inc., was sublimed at 150° (0.02 mm.) before use and was added in one portion.

7. The submitters reported a yield of 94–96 g. (97–98%). The spectral properties of the product are: infrared (neat) cm.^{-1} : 2151 and 1642; proton magnetic resonance (chloroform- d), δ (multiplicity, number of protons, assignment, coupling constant J in Hz.): 3.26 (singlet, 6, OCH_3), 4.78 (doublet, 1, $\text{CH}(\text{OCH}_3)_2$, $J = 8$), 5.60 (doublet, 1, vinyl CH , $J = 8$) and 7.45 (singlet, 5, aromatic H).

8. The intermediate vinyl azide should either be used immediately or else stored cold in a vented container since it slowly evolves nitrogen on standing at room temperature.

9. The reaction can be conveniently monitored by infrared spectroscopy by observing the intensity of the band at 2150 cm.^{-1} (N_3).

10. The spectral properties are: infrared (neat) cm.^{-1} : 1754 (azirine); proton magnetic resonance (chloroform- d), δ (multiplicity, number of protons, assignment, coupling constant J in Hz.): 2.38 (doublet, 1, vinyl CH in azirine ring, $J = 3$), 3.35 (singlet, 3, OCH_3), 3.47 (singlet, 3, OCH_3), 4.39 (doublet, 1, $\text{CH}(\text{OCH}_3)_2$, $J = 3$), 7.3–8.0 (multiplet, 5, aromatic H).

11. Dioxane available from Fisher Scientific Company was used without further purification.

12. The mixture is brought to 90° by heating at a rate of 1° per minute. The mixture *must not be overheated* or else the final product will be very difficult to crystallize.

13. Starting with 45.3 g. (0.24 mole) of the dimethyl acetal from Part C, the checkers obtained 10.2 g. (30%) of the product.

14. The submitters reported a yield of 35–38 g. (55–60%) based on 78–84 g. of starting material and using appropriate proportions of reagents. Their product had m.p. $45\text{--}47^\circ$. The spectral properties of the

azirine product are: infrared (KBr) cm^{-1} : 1786 and 1709; proton magnetic resonance (chloroform-*d*), δ (multiplicity, number of protons, assignment, coupling constant J in Hz.): 2.89 (doublet, 1, CH in azirine ring, $J = 7$), 7.5–8.0 (multiplet, 5, aromatic H), 9.04 (doublet, 1, aldehyde H, $J = 7$).

3. Discussion

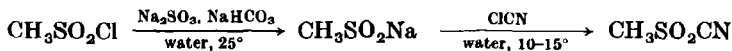
The formation of substituted azirines by the thermal decomposition of vinyl azides is a general reaction.³ The reagent iodine azide offers an excellent route to vinyl azides.^{4,5} Iodine azide adds to many olefinic compounds to give β -iodoazides which can easily eliminate hydrogen iodide upon treatment with base. The direction of iodine azide addition is consistent with electrophilic attack of $\text{I}^{\oplus}$ to give a cyclic iodonium ion which is opened by azide ion. The presence of the dimethylacetal moiety in the system above does not interfere with the iodine azide reaction. This procedure does not work with *trans*-cinnamaldehyde owing to a competing aldol condensation in the elimination step.

The aldehyde functionality present in 3-phenyl-2H-azirine-2-carboxaldehyde reacts selectively with amines and with Grignard and Wittig reagents to give a variety of substituted azirines.⁶ These azirines have been used, in turn, to prepare a wide assortment of heterocyclic rings such as oxazoles, imidazoles, pyrazoles, pyrroles, and benzazepins.^{6,7}

In addition to the present method, 2H-azirines can be prepared by using a modified Neber reaction,^{8–10} or by heating 4,5-dihydro-1,2,5-oxazaphospholes.^{11–14}

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SULFONYL CYANIDES: METHANESULFONYL CYANIDE



Submitted by M. S. A. VRIJLAND¹

Checked by Y. SUGIMURA and G. BÜCHI

1. Procedure

Caution! Since cyanogen chloride is highly toxic, the preparation and isolation of the sulfonyl cyanide should be conducted in a well-ventilated hood.

In a 2-l., three-necked, round-bottomed flask, equipped with a sealed mechanical stirrer, a pressure-equalizing dropping funnel capped with a gas outlet, and a thermometer, are placed 126 g. (0.50 mole) of sodium sulfite heptahydrate, 84.0 g. (1.00 mole) of sodium hydrogen carbonate, and 1 l. of water (Note 1). Stirring is begun, and 57.3 g. (0.50 mole) of freshly distilled methanesulfonyl chloride (Note 2) is added dropwise during 30 minutes. The slightly exothermic reaction is accompanied by the evolution of carbon dioxide. After stirring for 2 hours, gas evolution has ceased, and a clear, colorless solution of sodium methanesulfinate (Note 3) is obtained.

The dropping funnel is removed, the solution is cooled to 10° by the addition of ice, and 50 ml. (1.0 mole) of liquid cyanogen chloride (Note 4) is added in one portion with vigorous stirring. Addition of ice keeps the mixture at or below 15°. Within 1 minute the reaction mixture becomes turbid and methanesulfonyl cyanide separates as a heavy, colorless oil. The mixture is stirred for 15 minutes longer, and 200 ml. of benzene is added (Note 5). After 3 minutes of stirring, the layers are separated in a 2-l. separatory funnel, and the aqueous layer is extracted with two 100-ml. portions of benzene. The combined extracts are washed with water and dried overnight over anhydrous calcium chloride. Filtration and removal of solvent with a rotary evaporator *in a hood* affords an almost pure product (Note 6) which is distilled to yield 35.4–37.8 g. (67–72%) of methanesulfonyl cyanide, b.p. 68–69° (15 mm.), n_D^{20} 1.4301 (Note 7). Methanesulfonyl cyanide may be stored in a well-stoppered bottle, kept at or below 0°, for prolonged times without loss in purity (Note 8).

2. Notes

1. Excess sodium sulfite or sodium hydrogen carbonate should be avoided, since either would ~~react with the sulfonyl cyanide once formed.~~

2. The procedure given is applicable to many other sulfonyl chlorides as well (see Table I). Solid sulfonyl chlorides are added as such. When heavy frothing occurs in the reduction (*e.g.*, with *p*-nitrobenzenesulfonyl chloride), addition of 50 ml. of chloroform to the reaction mixture will eliminate the foam without reducing the final yield. When the sulfonyl chlorides were prepared according to Meerwein and co-workers,² it was found advantageous to use the crude, damp sulfonyl chlorides, since these are more easily reduced than the dried or recrystallized materials.

TABLE I
PREPARATION OF SULFONYL CYANIDES
FROM SULFONYL CHLORIDES^a

R =	RSO ₂ Cl from	m.p.	b.p.	Yield, %
Methyl	Commerce	—	68–69° (15 mm.)	72
Ethyl	RSCN + Cl ₂ ¹⁷	—	80–80.5° (18 mm.)	84
Propyl	R ₂ S ₂ + Cl ₂ ¹⁸	—	81–81.5° (18 mm.)	76
Benzyl	RSC(NH)NH ₂ ·HCl ¹⁹	89.5–91°		91
Cyclohexyl	RH + SO ₂ Cl ₂ ²⁰		72–73° (0.4 mm.)	85
<i>p</i> -Methoxyphenyl	RH + SO ₂ Cl ₂ ²¹	66–68°		88
<i>p</i> -Tolyl	Commerce	49.5–51°		89
Phenyl	Commerce	19–20°	118–119° (15 mm.)	92
<i>p</i> -Chlorophenyl	RN ₂ ⁺ Cl ⁻ + SO ₂ ²	57.5–59°		65 ^b
<i>p</i> -Cyanophenyl	RN ₂ ⁺ Cl ⁻ + SO ₂ ²	123–125°		79 ^b
<i>p</i> -Nitrophenyl	RN ₂ ⁺ Cl ⁻ + SO ₂ ²	122–123.5°		66 ^b

^a The preparations were performed on a 0.25 to 1-mole scale.

^b Overall yield from the corresponding aniline as starting material.

3. When crude sulfonyl chlorides were used as starting materials, the reaction mixture was washed with a suitable solvent to remove organic impurities. In the case of higher-melting crystalline sulfonyl chlorides, heating to 50° may be necessary to complete their reduction. The solution of the sulfinate salt may be kept overnight, if desired, with no decrease in the yield of sulfonyl cyanide.

4. Cyanogen chloride may be commercially available in gas cylinders.

It is liquefied by conducting the gas through a condenser cooled with ice water. Where difficult to obtain, it may be prepared by passing chlorine gas through a stirred suspension of sodium tetrakis(cyano-C)zincate prepared *in situ* from sodium cyanide and zinc sulfate.³

5. When the benzenesulfonates were substituted with electron-withdrawing groups, *e.g.*, *p*-nitro- and *p*-cyanobenzenesulfonate, the yields were slightly improved when the reaction time with cyanogen chloride was lengthened to 1 hour.

The higher-melting sulfonyl cyanides which separate as solids should be dried when dissolved in a suitable solvent, *e.g.*, benzene. *p*-Nitrobenzenesulfonyl cyanide is not readily extracted from the reaction mixture; it is collected on a Büchner funnel, pressed as dry as possible, dissolved in benzene, washed with water, and dried over anhydrous calcium chloride.

6. Solid sulfonyl cyanides now show a melting point not more than 1–2° below that of recrystallized material. They may be used without further purification. Analytically pure samples are obtained by recrystallization from dry benzene, dry petroleum ether, or a mixture of the two.

7. The product was further characterized as follows: infrared (liquid film) cm^{-1} : 2195 strong, 1370 strong, 1170 strong; proton magnetic resonance (chloroform-*d*) δ 3.43 (singlet).

8. Contrary to the findings of Cox and Ghosh,⁴ methanesulfonyl cyanide may be distilled without decomposition. Samples of benzene-, *p*-methoxybenzene-, and *p*-chlorobenzenesulfonyl cyanides were kept for over a year without loss in purity.

3. Discussion

Whereas sulfonyl halides have been known for a long time and, especially the chlorides, have become of great synthetic value, sulfonyl cyanides were unknown until 1968. They were first prepared by van Leusen and co-workers from the reaction of sulfonylmethylenephosphoranes with nitrosyl chloride.⁵ The same group also investigated part of their chemistry.^{6a-e} Since then, two more, completely different, methods of synthesis were published: from sulfinates with cyanogen chloride,⁴ and by the oxidation of thiocyanates.⁷

The procedure given above for the preparation of methanesulfonyl cyanide essentially is a combination of the sulfite reduction of a sulfonyl

chloride, as originally described by Bere and Smiles,⁸ and the sulfinate-cyanogen chloride reaction, first published by Cox and Ghosh.⁴

Some sulfinates are commercially available. They may be used as starting materials for the preparation of sulfonyl cyanides also. Yields, however, are not significantly better than when the much cheaper and more readily available sulfonyl chlorides are used as starting materials. Good to excellent results are obtained, even when starting from rather impure sulfonyl chlorides.⁹ Illustrative examples are given in Table I.

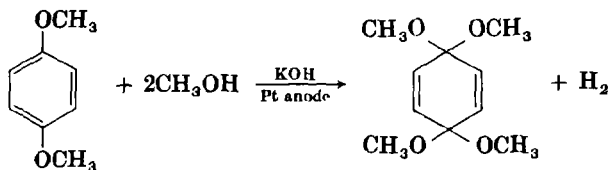
Sulfonyl cyanides have an activated cyano group and show many interesting reactions. With a range of *N*-, *O*-, *S*-, and *C*-nucleophiles, transfer of the cyano group to these nucleophiles is observed.^{6a,10,11} Hydroxylamine, hydrazine, and phenylhydrazine (α -effect nucleophiles) add to the cyano group of sulfonyl cyanides, yielding products that could be converted into substituted 1,2,4-oxadiazoles¹² and 1,2,4-triazoles,^{6a,10} respectively. Dienes show Diels-Alder cycloadditions with sulfonyl cyanides.^{6b-4,10,13} 1,3-Dipolar cycloadditions to the cyano group give rise to substituted tetrazoles (from azides), to substituted 1,2,3-triazoles (from diazo compounds), or to substituted 1,2,4-oxadiazoles (from nitrile *N*-oxides).^{6b,10} Sulfonyl cyanides undergo free-radical additions to alkenes.^{10,14} Chlorine and sulfonyl chlorides add to the cyano group of sulfonyl cyanides.^{15a,b,16}

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3,3,6,6-TETRAMETHOXY-1,4-CYCLOHEXADIENE

[1,4-Cyclohexadiene, 3,3,6,6-tetramethoxy-]



Submitted by PAUL MARGARETHA¹ and PAUL TISSOT²

Checked by RONALD F. SIELOFF and CARL R. JOHNSON

1. Procedure

A 600-ml., tall-form beaker is equipped with a thermometer, a magnetic stirring bar, and two electrodes. A 45-mesh cylindrical platinum anode (Note 1) is used. Surrounding the anode is a cylindrical nickel cathode (Note 2). The electrodes are held in place (distance between anode and cathode: 0.75 cm.) and suspended in the beaker by means of a clamp formed from Delrin rods (Note 3). The electrodes are connected to an adjustable d.c. power supply (Notes 4, 5).

A solution consisting of 27.6 g. (0.2 mole) of *p*-dimethoxybenzene (Note 6), 4.0 g. of potassium hydroxide, and 400 ml. of methanol is placed in the apparatus. The beaker and contents are cooled with a 0° bath. The solution is electrolyzed with magnetic stirring for 6 hours at a current intensity maintained at 2.0 A (Notes 5, 7). The temperature of the solution varies between 8° and 14°. During this time small amounts of methanol are added from time to time to compensate for evaporation.

After electrolysis the solution is reduced to a volume of 100 ml. in a

rotary evaporator and then extracted 10 times with 100-ml. portions of hexane. The hexane fractions are dried over anhydrous magnesium sulfate and the hexane evaporated on a rotary evaporator to yield white crystals, which are recrystallized from 75 ml. of pentane (Note 8) to afford 27.8–28.2 g. (70–71%) of pure 3,3,6,6-tetramethoxy-1,4-cyclohexadiene, m.p. 40–43° (Note 9).

2. Notes

1. The platinum anode used was Model 611 obtained from Engelhard Industries. This electrode has a height of 5.6 cm. and a diameter of 5.1 cm. The total surface area claimed by the supplier is 200 cm.².

2. The nickel cathode, fashioned from 22 gauge nickel sheet obtained from Huntington Alloys, Inc., Huntington, W. Va. 25720, had a height of 5.6 cm. and a diameter of 6.6 cm. When the sheet was rolled into a cylinder a small gap was left at the seam.

3. The clamp consisted of a 30 cm. vertical Delrin rod (0.5 cm. in diameter) threaded through the center of two 7-cm. horizontal Delrin rods (1.25 cm. in diameter). The horizontal rods were notched to hold the electrodes between them.

4. The power source used by the checkers was a 30-volt, 3-amp. adjustable d.c. supply.

5. The submitters used a cathode of nickel foil (140 × 71 × 0.5 mm.) rolled into a cylinder 3.5 cm. in diameter surrounded by three curved platinum anodes each having the dimensions 70 × 30 × 1 mm. (total surface area 130 cm.²) with a distance of 0.5–1 cm. between the cathode and the anodes. The submitters electrolyzed for 6 hours at a current maintained at 3.25 amp. This corresponds to a total of 19.5 amp.-hours and an anodic current density of 0.025 amp./cm.². Under these conditions the submitters report yields of 81–84%.

6. The *p*-dimethoxybenzene was obtained from Aldrich Chemical Company, Inc.

7. This corresponds to 12 amp.-hours (theoretical value is 10.6 amp.-hours). Longer electrolysis times did not significantly increase the yield of product.

8. Cooling is necessary in order to complete crystallization.

9. Proton magnetic resonance (chloroform-*d*) δ (multiplicity, number of protons, assignment): 3.30 (singlet, 12, OCH₃), 6.10 (singlet, 4, ring protons.)

3. Discussion

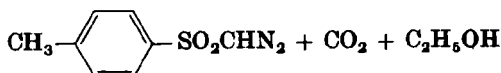
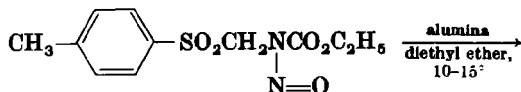
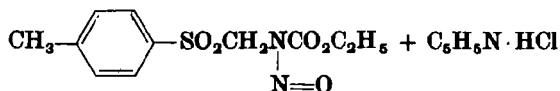
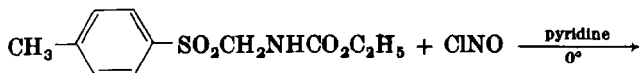
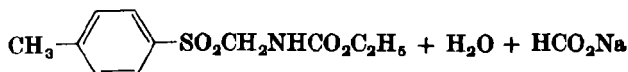
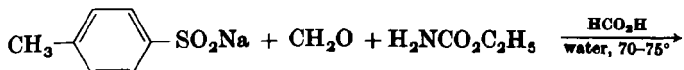
The procedure described is essentially that of Belleau and Weinberg³ and represents the only known way of obtaining the title compound. One other quinone acetal, 1,4,9,12-tetraoxadispiro[4.2.4.2]tetradeca-6,13-diene, has been synthesized by a conventional method (reaction of 1,4-cyclohexanedione with ethylene glycol followed by bromination and dehydrobromination⁴) as well as by an electrochemical method (anodic oxidation of 2,2-(1,4-phenylenedioxy)diethanol⁵). Quinone acetals have been used as intermediates in the synthesis of 4,4-dimethoxy-2,5-cyclohexadienone, *syn*-bishomoquinone,^{4,6} and compounds related to natural products.⁷

Aromatic ethers and furans undergo alkoxylation by addition upon electrolysis in an alcohol containing a suitable electrolyte.⁸⁻¹¹ Other compounds such as aromatic hydrocarbons, alkenes, *N*-alkyl amides, and ethers lead to alkoxyated products by substitution. Two mechanisms for these electrochemical alkoxyations are currently discussed. The first one consists of direct oxidation of the substrate to give the radical cation which reacts with the alcohol, followed by reoxidation of the intermediate radical and either alcoholysis or elimination of a proton to the final product. In the second mechanism the primary step is the oxidation of the alcoholate to give an alkoxyl radical which then reacts with the substrate, the consequent steps then being the same as above. The formation of quinone acetals in particular seems to proceed *via* the second mechanism.⁵

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***p*-TOLYLSULFONYLDIAZOMETHANE**

[Benzene, 1-[(diazomethyl)sulfonyl]-4-methyl-]



Submitted by A. M. VAN LEUSEN
and J. STRATING¹
Checked by BRUCE A. CARLSON
and WILLIAM A. SHEPPARD

1. Procedure

Caution! Part B must be conducted in an efficient hood to avoid exposure to toxic nitrosyl chloride.

A. *Ethyl N*-(*p*-tolylsulfonylmethyl)carbamate, [Carbamic acid, (4-methylphenylsulfonylmethyl)-, ethyl ester]. A solution of 178 g. (1.0 mole) of sodium *p*-toluenesulfinate (Note 1) in 1 l. of water is placed in a 3-l., three-necked flask, equipped with a condenser, an efficient mechanical stirrer, and a thermometer. After addition of 100 ml. (108 g.) of a 34–37% solution of formaldehyde (*ca.* 1.2–1.4 moles) (Note 2), 107 g. (1.2 moles) of ethyl carbamate (Note 3), and 250 ml. of formic acid (Note 4), the stirred solution is heated to 70°. Soon after this temperature is reached, the reaction mixture becomes turbid by separation of the

product in the form of oily droplets. The oil is kept in dispersed form by stirring vigorously. After heating for 2 hours at 70–75°, the heating mantle is replaced by an ice bath, while stirring is continued. At about 60° the product begins to solidify. Under continued stirring the mixture is cooled further and kept in the ice bath for 2 hours after a temperature of 5° is reached (Note 5). The precipitate is collected by suction filtration and is washed three times by stirring efficiently with 400-ml. portions of cold water. After drying at 70° to constant weight, 214–232 g. (83–90%) (see Note 1) of white, microcrystalline ethyl *N*-(*p*-toluenesulfonylmethyl)carbamate, m.p. 108–110°, is obtained; it is sufficiently pure for use in the next step of the reaction. Crystallization from 95% ethanol provides colorless flakes, m.p. 109–111°.

B. Ethyl *N*-nitroso-*N*-(*p*-tolylsulfonylmethyl)carbamate. A solution of 154 g. (0.60 mole) of the ethyl *N*-(*p*-tolylsulfonylmethyl)carbamate in 600 ml. of pyridine (Note 6) is placed in a 1-l., four-necked flask, equipped with a thermometer, a mechanical stirrer, a gas-inlet tube leading into the solution, and a gas-outlet leading to the exhaust. The weight of the flask together with its contents is determined, preferably on a balance placed in the same hood. The solution is cooled in an ice-salt mixture to 0°. Gaseous nitrosyl chloride (Note 7) is introduced, *via* a bubbler containing mineral oil and a trap, into the stirred solution at such a rate that the temperature is kept between 0° and 5°. After 52–65 g. (0.8–1.0 mole) of nitrosyl chloride has been taken up (Note 8), the reaction is completed by stirring for 30 minutes at about 0°. Then the reaction mixture is poured in a thin stream into a hand-stirred mixture of 4 l. of ice and water to give a pale-yellow oil that readily solidifies (Note 9). The solid is collected by suction filtration after standing for 1 hour at 0°. Any lumps present are pulverized and the solid is washed in a beaker thoroughly with four 500-ml. portions of cold water to remove pyridine. The moist product is dissolved in sufficient dichloromethane (*ca.* 1.5 l.) and the water layer is removed. The dichloromethane solution is dried over anhydrous magnesium sulfate and concentrated to dryness under reduced pressure, giving 157–171 g. (92–100%) of crude ethyl *N*-nitroso-*N*-(*p*-tolylsulfonylmethyl)carbamate, m.p. 86–89° (slight decomposition). The crude nitroso compound can be used without purification in the next step of the reaction, provided that it is free of starting material (Note 10).

If the nitrosocarbamate is to be stored (preferably at –20°) for periods longer than a month, it should be crystallized once from

dichloromethane-diethyl ether 1:2 (Note 11); the melting point is then 87–89°. In this purified form it can be stored for several months at –20° without noticeable decomposition.

C. *p*-Tolylsulfonyldiazomethane. *Warning!* α -Diazosulfones slowly decompose under the influence of light. Exposure to light should therefore be kept at a minimum in all stages of the reaction. In a 3-l., three-necked, round-bottomed flask, equipped with a condenser, an efficient mechanical stirrer, and a stopper, is placed 570 g. of alumina (Note 12). The flask is wrapped with aluminum foil or covered with dark cloth or black paper. The stirrer is started and 1.5 l. of diethyl ether (Note 13) is added. The mixture is cooled to 10–15° with a water-ice bath and a solution of 57.3 g. (0.20 mole) of ethyl *N*-nitroso-*N*-(*p*-tolylsulfonylmethyl)carbamate in 150 ml. of dichloromethane (Note 14) is added all at once. Stirring is continued for 2 hours at 10–15° (Note 15); during this time the ether solution soon develops the bright-yellow color of *p*-tolylsulfonyldiazomethane. The ether solution is decanted from the alumina. The alumina is extracted thoroughly by stirring for periods of 5 minutes with two portions of 500 ml., and three portions of 250 ml. of ether, successively. The combined ether solutions are filtered through a coarse paper filter and concentrated in a vacuum rotary flash evaporator. The temperature of the water bath must not exceed 25°. When the solution is concentrated to about 200 ml., the water bath is removed entirely and concentration is continued until the cold residue crystallizes spontaneously (Note 16). The crystal mass is stirred for about 2 minutes with 50 ml. of ice-cold petroleum ether (40–60°). The crystals are collected on a sintered-glass filter and are washed on the filter twice with 25-ml. portions of cold petroleum ether. After drying overnight at 0° in a vacuum dessiccator over anhydrous calcium chloride, 26–30 g. (66–76%) of yellow *p*-tolylsulfonyldiazomethane is obtained, m.p. 35–38° (slight decomposition) (Note 17). Crystallization from anhydrous ether-pentane (Note 18) will raise the melting point to 36–38° (slight decomposition) at the expense of 5–10% of material. *p*-Tolylsulfonyldiazomethane should be stored at or below 0° in the absence of light and in an *unsealed* container (Note 19).

2. Notes

1. Commercially available anhydrous sodium *p*-toluenesulfinate, purum, ca. 97% (Fluka A G, Busch S.G., Switzerland) was used.

Sodium *p*-toluenesulfinate dihydrate can be used equally well. The checkers used anhydrous sodium *p*-toluenesulfinate from Aldrich Chemical Company, Inc. This material was determined by titration to be 87% pure and gave lower yields. The yield stated was obtained by using stoichiometric amounts based on calculated purity. Sodium *p*-toluenesulfinate from other suppliers was found less pure and gave considerably lower yields.

Alternatively, sulfonates can be synthesized conveniently by the method of Truce and Roberts², or by the method of Oxley and colleagues.³

2. Commercial aqueous formaldehyde solution, containing about 8% of methanol, was used.

3. Ethyl carbamate (J. T. Baker Chemical Company), melting point reported to be 48–50° (but 46–49° was found) was used without purification. The solid was added to the reaction mixture.

4. Formic acid (97%) from J. T. Baker Chemical Company was used.

5. By cooling and stirring as described, the product is obtained in a finely divided form, which can be removed from the flask easily and also can be washed efficiently.

6. Commercial pyridine (J. T. Baker Chemical Company) was used without purification.

7. Nitrosyl chloride (Matheson Gas Products) with a purity specified as >97% was used. Occasionally, the needle valve of the nitrosyl chloride tank clogs. After closing the tank, the valve is disconnected and flushed with acetone until the acetone remains colorless. The needle valve is reconnected after being dried with compressed air.

Nitrosyl chloride also can be prepared conveniently from hydrochloric acid and sodium nitrite.⁴

8. The color of the pyridine solution changes rapidly from blue and green to yellow. After roughly 1 equivalent (0.6 mole) of nitrosyl chloride has been taken up (this takes about 1 hour), the color of the solution changes to dark red-brown. During the reaction a precipitate of pyridinium chloride is formed which, however, will disappear during the work-up with water as described in the text. A larger excess of nitrosyl chloride (up to 3 equivalents) has been used occasionally without any disadvantages.

9. Preferably, a few drops of the pyridine solution are rubbed first with a little water to provide seeding crystals so that the product will

solidify immediately to give a finely divided material which can be washed more easily.

10. The presence of ethyl *N*-(*p*-tolylsulfonylmethyl)carbamate in the reaction product is most readily detected by the N-H infrared absorption band at 3370 cm.^{-1} . If the nitrosation is incomplete, the reaction with nitrosyl chloride should be repeated on the mixture of compounds, rather than to try and purify the product by crystallization.

11. Diethyl ether (about 1.4 l.) is added to a warm filtered solution of 100 g. of the crude nitroso compound in *ca.* 0.7 l. of dichloromethane until the solution becomes slightly turbid. The nitrosocarbamate is collected after cooling overnight at -20° , and is dried under reduced pressure at 0° , providing 88–93 g. of yellow crystals with a pink luster, m.p. 87–89.

12. Alumina Number 1076, "aktiv basisch," for chromatography (E. Merck, Darmstadt) was usually employed. Occasionally, when alumina Number 1077, "aktiv neutral," from the same company, was used, a longer reaction time was required (compare Note 15).

13. Commerical ether was stored over potassium hydroxide pellets and used without being distilled. Because some heat is evolved when the ether is added to the alumina, the flask is equipped with a condenser.

14. Commercial dichloromethane was used without purification.

15. The time necessary for completion of the reaction may vary from 0.5 to 4 hours, depending on the actual activity of the alumina. The progress of conversion should be monitored by infrared analysis of a concentrated sample of the solution. Stirring should be continued for 15 minutes after the nitroso band at 1540 cm.^{-1} has disappeared. A strong diazo band at about 2100 cm.^{-1} will then be present. The carbonyl band at 1750 cm.^{-1} , initially due to nitrosocarbamate, will usually not disappear completely during the reaction, because some diethyl carbonate is formed in addition to carbon dioxide and ethanol. Diethyl carbonate is removed during the work-up procedure.

During the reaction the alumina usually attains a pink color which is due to some decomposition of *p*-tolylsulfonyldiazomethane. However, the colored decomposition products adhere strongly to the alumina and will therefore not contaminate the final product. If the alumina becomes reddish rather than pink, the type of the alumina in use may be too basic, causing more extensive decomposition of the *p*-tolylsulfonyldiazomethane; the reaction time should then be reduced as much as possible to prevent a considerable decrease in yield.

16. If crystallization does not occur, it can be induced readily by scratching.

17. Spectral data of *p*-tolylsulfonyldiazomethane are: infrared (Nujol) cm.^{-1} : 2125 ($\text{C}\equiv\text{N}=\text{N}$), 1330 (SO_2), 1150 (SO_2); proton magnetic resonance (chloroform-*d*) δ (multiplicity, number of protons, assignment): 2.46 (singlet, 3, CH_3), 5.36 (singlet, 1, CH), 7.30, 7.43, 7.73, 7.87 (AB quartet, 4, aromatic CH); visible (40% dioxane-water) nm. max. ($\log \epsilon$): 394 (1.8).

18. *p*-Tolylsulfonyldiazomethane tends to separate as an oil when pentane is in excess of the ratio of ether to pentane of 2:1. The *p*-tolylsulfonyldiazomethane is dissolved at room temperature in anhydrous ether (about 20 ml. per 10 g. of *p*-tolylsulfonyldiazomethane), and pentane (about 7 ml. per 10 g.) is added, followed by seeding crystals. The solution is cooled first at 0° , then at -20° , before the crystals are collected.

19. *p*-Tolylsulfonyldiazomethane is insensitive to impact detonation. However, it decomposes on warming, evolving significant quantities of nitrogen as low as 32° . It should never be stored for any length of time in a sealed container, and it should be stored at or below 0° if not used immediately.

3. Discussion

p-Tolylsulfonyldiazomethane (diazomethyl *p*-tolyl sulfone) represents a class of compounds called α -diazosulfones, which was discovered in 1961 by the submitters. Besides being useful synthetic intermediates, α -diazosulfones are the only known source of α -sulfonylcarbenes.⁵

Several new trisubstituted methane derivatives have been prepared by replacing the diazo group in α -diazosulfones.⁵ For example, *p*-tolylsulfonyldiazomethane (RSO_2CHN_2 , $\text{R} = p\text{-tolyl}$ throughout) reacts: with *p*-toluenesulfonyl chloride⁶ to give chloro-*p*-tolylsulfonyl-*p*-tolylthiomethane [$\text{RSO}_2\text{CH}(\text{Cl})\text{SR}$] in 83% yield;⁷ with nitrosyl chloride to yield the previously unknown *N*-hydroxy-1-(*p*-tolylsulfonyl)-methanimidoyl chloride [$\text{RSO}_2\text{C}(\text{Cl})=\text{NOH}$, 28% yield];⁸ with 70% aqueous perchloric acid in dichloromethane to give the isolable covalent perchlorate $\text{RSO}_2\text{CH}_2\text{OCIO}_3$ (49% yield);^{9,5} and with *tert*-butyl hypochlorite in *tert*-butyl alcohol to give 1-(1-*tert*-butoxy-1-chloromethylsulfonyl)-4-methylbenzene [$\text{RSO}_2\text{CH}(\text{Cl})\text{OC}(\text{CH}_3)_3$, 62%] or 1-(1-chloro-1-ethoxymethylsulfonyl)-4-methylbenzene [$\text{RSO}_2\text{CH}(\text{Cl})\text{OC}_2\text{H}_5$, 84%] when carried out in ethanol.¹⁰

The photolysis of α -diazosulfones dissolved in alkenes provides sulfonyl-substituted cyclopropanes in high yields.⁵ This is exemplified by the preparation of 1-(*p*-methoxyphenylsulfonyl)-2,2,3,3-tetramethylcyclopropane in 75% yield from *p*-methoxybenzenesulfonyldiazomethane and 2,3-dimethyl-2-butene. A similar addition to *trans*-2-butene gives (*d, l*)-1-(*p*-methoxyphenylsulfonyl)-*trans*-2,3-dimethylcyclopropane in 79% yield, resulting from a stereospecific *cis* addition, thus indicating a singlet sulfonylcarbene intermediate.¹¹

Originally, *p*-tolylsulfonyldiazomethane was prepared by passing an ethereal solution of its precursor, ethyl *N*-nitroso-*N*-(*p*-tolylsulfonylmethyl)carbamate, slowly through a column of alumina.¹² This procedure, which results in yields about 10% higher, is convenient only for small-scale preparations, up to a maximum of 5 g. of *p*-tolylsulfonyldiazomethane. The present modification is due to Middelbos.¹³

The conversion of nitrosocarbamates into α -diazosulfones is effected also with certain bases, notably by aqueous potassium hydroxide.¹² Potassium hydroxide, however, causes rapid decomposition of *p*-tolylsulfonyldiazomethane. Alumina is thought to act as a solid base and does not cause significant decomposition.

Other syntheses of *p*-tolylsulfonyldiazomethane have been worked out. Reaction of *p*-carboxybenzenesulfonyl azide and ammonia with *p*-tolylsulfonylacetaldehyde hemihydrate or *p*-tolylsulfonylacetaldehyde enol acetate gives *p*-tolylsulfonyldiazomethane in yields of 73 and 58%, respectively.¹⁴ Furthermore, *p*-tolylsulfonyldiazomethane is obtained in 60% yield by reaction of *p*-tolylsulfonylmethylenetriphenylphosphorane and either *p*-tolylsulfonyl azide or *p*-carboxybenzenesulfonyl azide.¹⁴ A method similar to the first of these syntheses has been used for preparation of (alkyl- or arylsulfonyl)phenyldiazomethanes. However, the present procedure has the advantage of being simple and easily scaled-up, and uses readily available, inexpensive starting materials.

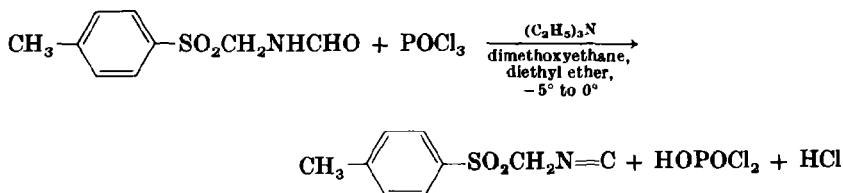
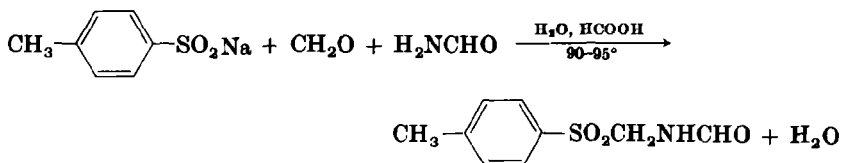
An alternative to the synthesis of arylsulfonylmethylcarbamates by the Mannich condensation as described here,¹⁵ is the Curtius rearrangement of the hydrazides of arylsulfonylacetic acids.¹⁶

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***p*-TOLYLSULFONYLMETHYL ISOCYANIDE**

[Benzene, 1-((isocyanomethyl)sulfonyl)-4-methyl-]



Submitted by B. E. HOOGENBOOM, O. H. OLDENZIEL,
and A. M. VAN LEUSEN¹

Checked by TERESA Y. L. CHAN and S. MASAMUNE

1. Procedure

Caution! The reaction should be conducted in a well-ventilated fume hood.

A. N-(*p*-Tolylsulfonylmethyl)formamide [Formamide, N-(4-methyl-

phenylsulfonylmethyl]-].² A 3-l., three-necked, round-bottomed flask, equipped with a mechanical stirrer, a condenser, and a thermometer, is charged with 267 g. (1.5 moles) of sodium *p*-toluenesulfinate (Note 1). After addition of 750 ml. of water, 350 ml. (378 g.) of a 34–37% solution of formaldehyde (*ca.* 4.4 moles) (Note 2), 600 ml. (680 g., 15 moles) of formamide (Note 3), and 200 ml. (244 g., 5.3 moles) of formic acid (Note 4), the stirred reaction mixture is heated at 90°. The sodium *p*-toluenesulfinate dissolves during heating, and the clear solution is kept at 90–95° for 2 hours (Note 5). The reaction mixture is cooled to room temperature in an ice-salt bath with continued stirring and then further cooled overnight in a freezer at –20°. The white solid (Note 6) is collected by suction filtration. It is washed thoroughly in a beaker by stirring with three 250-ml. portions of ice water. The product is dried under reduced pressure over phosphorus pentoxide at 70° (Note 7) to provide 134–150 g. (42–47%) of crude *N*-(*p*-tolylsulfonylmethyl)-formamide, m.p. 106–110° (Note 8). This product is sufficiently pure to be used directly in the next step of the reaction.

B. *p*-Tolylsulfonylmethyl isocyanide. A 3-l., four-necked, round-bottomed flask, equipped with a mechanical stirrer, a thermometer, a 250-ml. dropping funnel, and a drying tube, is charged with 107 g. (0.50 mole) of crude *N*-(*p*-tolylsulfonylmethyl)formamide, 250 ml. of 1,2-dimethoxyethane, 100 ml. of anhydrous ether, and 350 ml. (255 g., 2.5 moles) of triethylamine (Note 9). The stirred suspension is cooled in an ice-salt bath to –5°. A solution of 50 ml. (84 g., 0.55 mole) of phosphorus oxytrichloride (phosphoryl chloride) (Note 10) in 60 ml. of 1,2-dimethoxyethane is then added from the dropping funnel at such a rate that the temperature is kept between –5° and 0° (Note 11). During the reaction the *N*-(*p*-tolylsulfonylmethyl)formamide gradually dissolves and triethylamine salts precipitate. Near the completion of the reaction the white suspension slowly turns brown (Note 12). After stirring for another 30 minutes at 0°, 1.5 l. of ice water is added with continued stirring. The solid material dissolves to give a clear, dark-brown solution before the product begins to separate as a fine, brown crystalline solid. After stirring for 30 minutes at 0°, the precipitate is collected by suction filtration and washed with 250 ml. of cold water. The wet product is dissolved in 400 ml. of warm benzene (40–60°), the aqueous layer is removed with a separatory funnel, and the dark-brown benzene solution is dried over anhydrous magnesium sulfate. After removal of the magnesium sulfate, 2 g. of activated carbon (Note 13) is added, the mixture

is heated at about 60° for 5 minutes and then filtered (Note 14). One liter of petroleum ether (b.p. 40–60°) is added to the filtrate with thorough swirling. After 30 minutes the precipitate is collected by suction filtration and dried in a vacuum desiccator to give 74–82 g. (76–84%) of crude *p*-tolylsulfonylmethyl isocyanide as a light-brown odorless solid, m.p. 111–114° (dec.) (Note 15). This material can be used for synthetic purposes without further purification.

Completely white material is obtained by rapid chromatography through alumina (Note 16). An analytically pure product, m.p. 116–117° (dec.), is obtained after one crystallization from methanol.

2. Notes

1. The submitters used anhydrous sodium *p*-toluenesulfinate ("purum" quality, *ca.* 97% from Fluka A G), and the checkers purchased the reagent from Aldrich Chemical Company, Inc.

2. Commercial aqueous formaldehyde solution containing 8% methanol was used. Formaldehyde is needed in excess; otherwise the yield is considerably diminished.

3. Commercial formamide (E. Merck, Darmstadt) was used. The use of a large excess of formamide with respect to the sulfinate is required in order to obtain the yield specified.²

4. Commercial 97% formic acid (J. T. Baker Chemical Company) was used.

5. Prolonged heating lowers the yield considerably.

6. When no solid is formed overnight, crystallization may be induced by scratching. In this case the solution should be kept for another 4 hours at –20° before the product is collected.

7. The drying process can be speeded up by dissolving the wet product in dichloromethane, removing the water layer in a separatory funnel, drying the dichloromethane solution over anhydrous magnesium sulfate, and removing the solvent on a rotary evaporator.

8. Recrystallization from 95% ethanol or benzene raised the m.p. to 108–110°.

9. 1,2-Dimethoxyethane and triethylamine, both in "zur Synthese" quality, were purchased from E. Merck, Darmstadt. Diethyl ether was distilled from phosphorus pentoxide and stored over sodium wire.

10. Commercial phosphorus oxytrichloride ("tout pur" from UCB, Belgium) was used without purification.

11. The addition requires about 1 hour. At the beginning of the reaction much heat is evolved, and therefore the phosphorus oxytrichloride solution should initially be added very slowly.

12. The development of a brown color indicates that sufficient phosphorus oxytrichloride has been added. If the mixture remains colorless, the final product is likely to be contaminated with unreacted *N*-(*p*-tolylsulfonylmethyl)formamide. It is therefore advantageous to add more phosphorus oxytrichloride and continue stirring until the brown color is obtained.

13. Purchased from J. T. Baker Chemical Company.

14. The color of the solution is lightened only slightly by treatment with activated carbon, but eventually a purer product is obtained.

15. The product has the following spectral properties; infrared (Nujol) cm.^{-1} : 2150 ($\text{N}=\text{C}$), 1320 and 1155 (SO_2); proton magnetic resonance (chloroform-*d*) δ (multiplicity, number of protons, assignment): 2.5 (singlet, 3, CH_3), 4.6 (singlet, 2, CH_2), 7.7 (quartet, 4, aromatic).

16. A solution of 50 g. of *p*-tolylsulfonylmethyl isocyanide in 150 ml. of dichloromethane is placed on a 40×3 cm. column containing about 100 g. of neutral alumina slurried in dichloromethane. A nearly colorless solution (ca. 700 ml.) is collected over about 1 hour. This solution is evaporated to dryness on a rotary evaporator, providing 42–47 g. of white *p*-tolylsulfonylmethyl isocyanide, m.p. 113–114° (dec.).

3. Discussion

p-Tolylsulfonylmethyl isocyanide was originally obtained by irradiation of *p*-tolylsulfonyldiazomethane³ in liquid hydrogen cyanide.⁴ This isocyanide represents a group of sulfonylmethyl isocyanides, most of which have been prepared, as in the present procedure, by dehydration of the corresponding formamides.^{4,5} *p*-Tolylsulfonylmethyl isocyanide has also been prepared by reaction of *p*-tolylsulfonyl fluoride with isocyanomethyl lithium.^{4,6} The advantages of the present dehydration method are twofold: (1) it is a simple procedure using readily available and inexpensive starting materials and (2) the use of the foul-smelling methyl isocyanide is avoided.

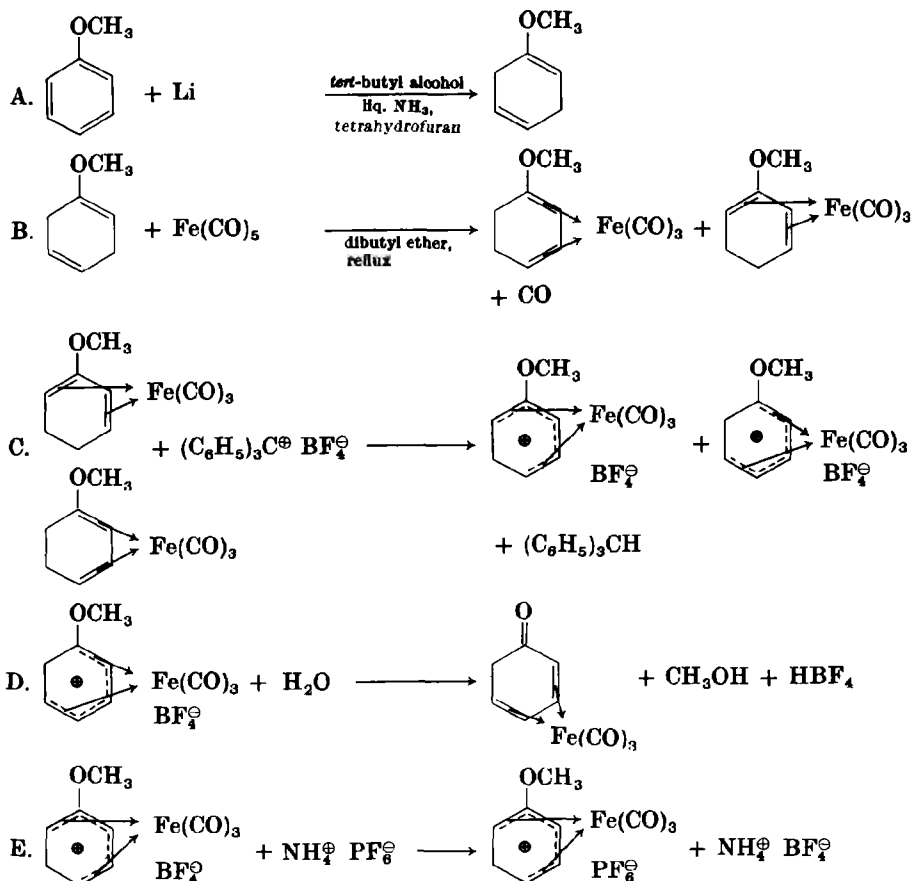
p-Tolylsulfonylmethyl isocyanide is a useful and versatile reagent in organic chemistry. It has been used for the synthesis of several azole ring systems by base-induced addition of its $\text{C}=\text{N}=\text{C}$ moiety to various

C=O, C=N, C=S, C=C, and N≡N containing substrates. Thus oxazoles,⁷ imidazoles,⁸ thiazoles,⁹ pyrroles,¹⁰ and 1,2,4-triazoles¹¹ have been prepared, respectively. Furthermore, *p*-tolylsulfonylmethyl isocyanide has found use in a one-step conversion of ketones into cyanides¹²⁻¹⁴ and in a two-step synthesis of α -hydroxyaldehydes from ketones.¹⁵

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**TRICARBONYL[(2,3,4,5- η)-2,4-CYCLOHEXADIEN-1-ONE]IRON AND
TRICARBONYL[(1,2,3,4,5- η)-2-METHOXY-2,4-CYCLOHEXADIEN-
1-YL]IRON(1+) HEXAFLUOROPHOSPHATE(1-) FROM ANISOLE**

[Iron, tricarbonyl[(2,3,4,5- η)-2,4-cyclohexadien-1-one] and Iron(1+),
tricarbonyl[(1,2,3,4,5- η)-2-methoxy-2,4-cyclohexadien-1-yl]
hexafluorophosphate (1-)]



Submitted by A. J. BIRCH and K. B. CHAMBERLAIN¹
Checked by SUSUMU KAMATA, TSUTOMU AOKI,
and WATARU NAGATA

1. Procedure

Caution! Parts A and B must be conducted in an efficient hood to prevent exposure to ammonia, iron pentacarbonyl, and carbon monoxide.

A. *1-Methoxy-1,4-cyclohexadiene*. A 3-l., three-necked, round-bottomed flask equipped with an inlet tube, mechanical stirrer, and dry-ice condenser (cooled with acetone-dry ice) fitted with a drying tube, is charged with 150 ml. of tetrahydrofuran, 250 ml. of *tert*-butyl alcohol, and 50 g. (0.46 mole) of anisole (Note 1). About 1.5 l. of dried liquid ammonia (Note 2) is distilled into the reaction vessel from a steam bath. Lithium (11.5 g., 1.66 g.-atoms) (Notes 3, 4) is added cautiously with stirring and, when the addition is complete, the stirring is continued for 1 hour with refluxing. The blue color is discharged by cautiously adding methanol dropwise (about 100 ml. is required); then 750 ml. of water is carefully added. The excess ammonia is allowed to evaporate overnight, more water is added to dissolve the lithium salts, and the mixture is extracted three times with 100-ml. portions of petroleum ether (b.p. 30–40°) (Note 5). The combined extracts are washed four times with 75-ml. portions of water to remove *tert*-butyl alcohol and methanol, dried over anhydrous magnesium sulfate, and the solvent is removed through a 30-cm. Vigreux column (Note 6) under reduced pressure (20 mm.). The residue on distillation yields 1-methoxy-1,4-cyclohexadiene (38–40 g., about 75%) (Notes 7, 8), b.p. 40° (20 mm.).

B. *Tricarbonyl[(1,2,3,4- η)-1- and 2-methoxy-1,3-cyclohexadiene]iron*. A 500-ml., three-necked, round-bottomed flask equipped with a nitrogen-inlet tube, a condenser provided with a gas bubbler, and a stopper is flushed with nitrogen and is charged with 39 g. (0.35 mole) of 1-methoxy-1,4-cyclohexadiene, 320 ml. of dibutyl ether (Note 9), and 95 g. (65 ml., 0.49 mole) of filtered iron pentacarbonyl (Notes 10–12). Using a heating mantle, the mixture is refluxed for 18 hours (Note 13) under a slow nitrogen stream. After cooling, the reaction mixture is filtered by suction through Celite to remove iron particles (Note 14), the Celite is washed twice with 15-ml. portions of dibutyl ether, and the washings and filtrate are combined. The crude product (Note 15) is obtained by evaporating excess iron pentacarbonyl, unreacted diene, and the dibutyl ether using a rotary evaporator (in a fume hood), with a hot-water bath and ice cooling of the receiver. The distillate is again refluxed for 18 hours under nitrogen as before and worked up in the same manner.

This procedure is then repeated again. Distillation of the combined residues using a nitrogen leak (Note 16) yields 54 g. of the product as a yellow oil, b.p. 66–68° (1.1 mm.) (Note 17). The distillation residue, when washed through a short acidic alumina column with light petroleum ether and the solvent evaporated, yields an additional 5 g. of product; total yield 59–68 g., 67–78% (Notes 18, 19).

C. *Tricarbonyl*[(1,2,3,4,5- η)-1-and 2-methoxy-2,4-cyclohexadien-1-yl]-*iron*(1+) *tetrafluoroborate*(1-). Triphenylmethyl tetrafluoroborate [Methylum, triphenyl]-, tetrafluoroborate] (34 g., 0.103 mole) (Note 20) is dissolved in a minimum volume of dichloromethane and 18 g. (0.072 mole) of tricarbonyl (1- and 2-methoxy-1,3-cyclohexadiene)iron dissolved in a like volume of dichloromethane is added. The resulting dark solution is left for 20–30 minutes and then added with stirring to three times its volume of ether (Note 21). The precipitate is collected and washed with ether to yield 21–22 g. (87–91%) of product as yellow solid (Note 19).

D. *Tricarbonyl*[(2,3,4,5- η)-2,4-cyclohexadien-1-one]*iron*. The mixture of tetrafluoroborate from Part C (21 g., 0.062 mole) is heated on a steam bath for 1 hour in 450 ml. of water, during which time orange crystals separate. After cooling, the mixture is extracted three times with 100-ml. portions of ether into which most of the solid dissolves. (The aqueous layer is used in Part E.) The extracts are dried over anhydrous magnesium sulfate, and the ether is evaporated to yield the yellow crystalline dienone complex, 7–7.5 g. (47–51%) (Note 22).

E. *Tricarbonyl*[(1,2,3,4,5- η)-2-methoxy-2,4-cyclohexadien-1-yl]-*iron*(1+) *Hexafluorophosphate*(1-). To the aqueous layer from Part D is added with swirling 7.1 g. (0.044 mole) of ammonium hexafluorophosphate (Note 23) in 30 ml. water. After 30 minutes, the light-yellow product is filtered, washed with water, and air dried; the yield is about 9–10 g. (35–44%) (Notes 19, 24).

2. Notes

1. Anisole (500 g.) was purified² by washing twice with 50 ml. of 2*N* sodium hydroxide, twice with 50 ml. of water, drying over anhydrous magnesium sulfate, and distillation, b.p. 43–46° (20 mm.). The checkers used anisole obtained from Kanto Chemical Co., Ltd., Japan.

2. Liquid ammonia from a cylinder is purified by addition of 2–3 g. of sodium cut into small pieces, and distilled into the reaction vessel.

3. The submitters used lithium wire (Merck & Company, Inc.) (12 in. = 1 g.) cut into small pieces for addition to the ammonia solution. The checkers used a block of lithium cut into small pieces.

4. The lithium pieces must be small and added to the ammonia solution cautiously. If too much is added at one time, the reaction becomes violent and froths.

5. Frequently not all of the ammonia evaporates; the first extraction should be by swirling in a separatory funnel without a stopper, and subsequent extractions should be done with frequent pressure release.

6. The solvent must be carefully removed; use of a rotary evaporator results in considerable loss of the product.

7. The infrared spectrum of the 1-methoxy-1,4-cyclohexadiene shows the absence of strong aromatic absorption at 1600 cm.^{-1} ; the ultraviolet spectrum shows absence of absorption at 270 nm. , indicating absence of the conjugated isomer.

8. Proton magnetic resonance spectrum δ (number of protons): 2.5–2.9 (4), 2.48 (3), 3.50 (1), 5.60 (2).

9. The dibutyl ether must be dry and peroxide-free. This can be achieved by filtering it through a large column of basic alumina, or by leaving overnight over sodium wire and distillation. If these precautions are not observed, low yields result. The checkers purified dibutyl ether by distillation from sodium hydride dispersion.

10. During the reaction the hood must be operating at all times as carbon monoxide is evolved.

11. Iron pentacarbonyl is toxic and volatile; consequently, it should only be handled in a good hood, while wearing gloves.

12. The submitters used iron pentacarbonyl "pract." grade obtained from Fluka A G. The checkers used iron pentacarbonyl obtained from Merck, Germany.

13. When the reaction was followed by proton magnetic resonance, it was found that the yield reached a maximum after 18 hours; longer refluxing resulted in decomposition and lower yields. At this time, also, the maximum proportion of the 1-methoxy isomer was produced; this isomer is converted into the dienone complex.

14. Care should be exercised in filtering the reaction mixture. The solid collected is largely finely divided iron and is pyrophoric, so it should not be allowed to dry.

15. The crude product is unstable; it should be stored under nitrogen with refrigeration.

16. Alternatively, rapid magnetic stirring will prevent bumping and allow distillation without using a gas bleed.

17. For smaller batches, purification by washing the product through a short column of acidic alumina with light petroleum ether and evaporation of the solvent is satisfactory.

18. In one of the checker's experiments almost all the material could be distilled, giving 68.14 g. (77.9%) of the product, b.p. 66–67° (0.3–0.4 mm.).

19. For proton magnetic resonance and infrared spectra, see Birch and co-workers.³

20. Triphenylmethyl fluoroborate is prepared by dissolving 27 g. (0.104 mole) of triphenylmethanol ("purum," Fluka A G) in 260 ml. of propionic anhydride by warming on a steam bath. With an acetone–dry ice bath the solution is cooled to 10° and maintained between 10° and 20° while 31 ml. of 43% w/w fluoroboric acid is added portionwise with swirling. The yellow solid is collected, washed well with dry ether, and dried in a desiccator under vacuum to yield 34 g. (90–99%). The product is very hygroscopic, taking up water with hydrolysis. It is desirable to prepare this reagent immediately before use.

21. The ether should be reagent grade but not sodium-dried. The traces of water present destroy excess reagent, leading to a cleaner product.

22. The product at this stage is sufficiently pure for most purposes. It can be recrystallized in small batches from water³ and has m.p. 104–104.5°; it can be chromatographed on silica or acidic alumina or sublimed at 80–90° (0.2 mm.). The checkers obtained the purified material (m.p. 104–105°) by recrystallization from dichloromethane–ether. The purified material has the following spectral data: infrared spectrum (chloroform) cm^{-1} : 2070 strong, 2000 strong, 1665 strong; proton magnetic resonance spectra (chloroform-*d*), δ (multiplicity, number of protons): 2.28–2.45 (multiplet, 2), 3.1–3.46 (multiplet, 2), 5.6–6.1 (multiplet, 2).

23. Obtained from Ozark-Mahoning Chemical Co.

24. The complex can be stored for long periods under nitrogen in a refrigerator with only slight darkening. The purified material has the spectral data: infrared spectrum (Nujol) cm^{-1} : 2110 strong, 2060 strong, 1515 weak, 1494 weak, 1253 medium strong.

3. Discussion

Anisole is reduced using the solvent system of Dryden and colleagues.⁴

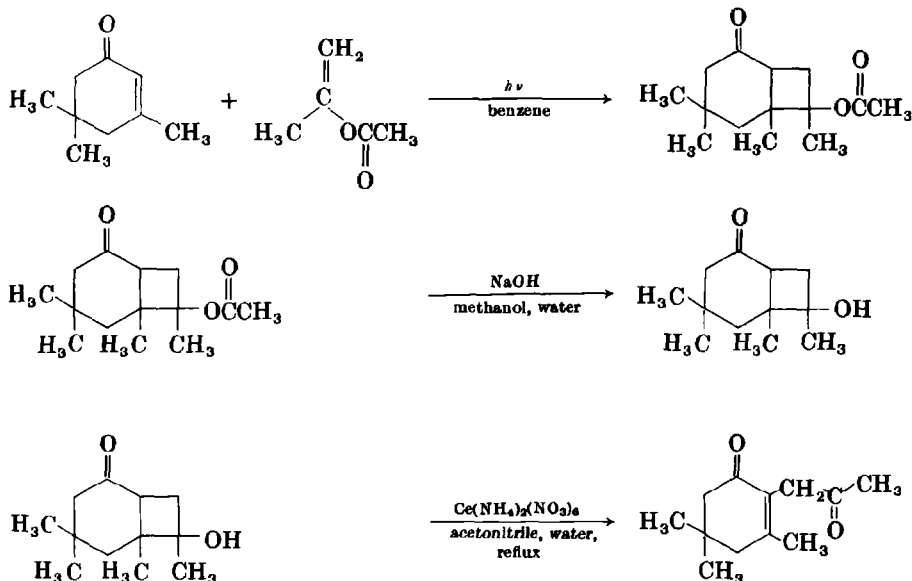
Iron pentacarbonyl and 1-methoxy-1,4-cyclohexadiene react as shown by Birch and co-workers,³ but in dibutyl ether; this solvent has been found superior.⁵ The tricarbonyl(methoxy-1,3-cyclohexadiene)iron isomers undergo hydride abstraction^{3,6} with triphenylmethyl tetrafluoroborate to form the dienyl salt mixture of which the 1-methoxy isomer is hydrolyzed by water to the cyclohexadienone complex. The 2-methoxy isomer can be recovered by precipitation as the hexafluorophosphate salt. By this method the 3-methyl-substituted dienone complex has also been prepared³ from 1-methoxy-3-methylbenzene. The use of the conjugated 1-methoxy-1,3-cyclohexadiene in Part B led to no increase in yield or rate and resulted chiefly in another product of higher molecular weight. An alternative procedure for the dienone is to react tricarbonyl(1,4-dimethoxycyclohexadiene)iron with sulfuric acid.⁷

The dienone complex is an effective phenylating agent for aromatic amines; *e.g.*, aniline and tricarbonylcyclohexadienoneiron in glacial acetic acid at 75° overnight gives diphenylamine in 95% yield.⁸

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3,5,5-TRIMETHYL-2-(2-OXOPROPYL)-2-CYCLOHEXEN-1-ONE

[2-Cyclohexen-1-one, 3,5,5-trimethyl-2-(2-oxopropyl)-]



Submitted by Z. VALENTA¹ and H. J. LIU²

Checked by T. H. O'NEILL, W. THOMPSON, D. H. LAWKE,
and R. E. IRELAND

1. Procedure

The apparatus used for the photocycloaddition reaction is shown in Figure 1. In the reaction vessel is placed a solution of 34.5 g. (0.25 mole) of 3,5,5-trimethyl-2-cyclohexen-1-one (isophorone) (Note 1) and 500 g. (5 moles) (Note 2) of isopropenyl acetate (Note 3) in 625 ml. of benzene. A constant and moderate flow of argon (Note 4) is maintained to agitate the solution throughout the reaction period. The trap is filled with isopropyl alcohol-dry ice (Note 5). The solution is irradiated with a 450-watt Hanovia high-pressure quartz mercury vapor lamp using a Pyrex filter for 96 hours (Note 6). Concentration of the resultant solution under reduced pressure (water aspirator) gives 65-80 g. of crude 7-acetoxy-4,4,6,7-tetramethylbicyclo[4.2.0]octan-2-one (Note 7).

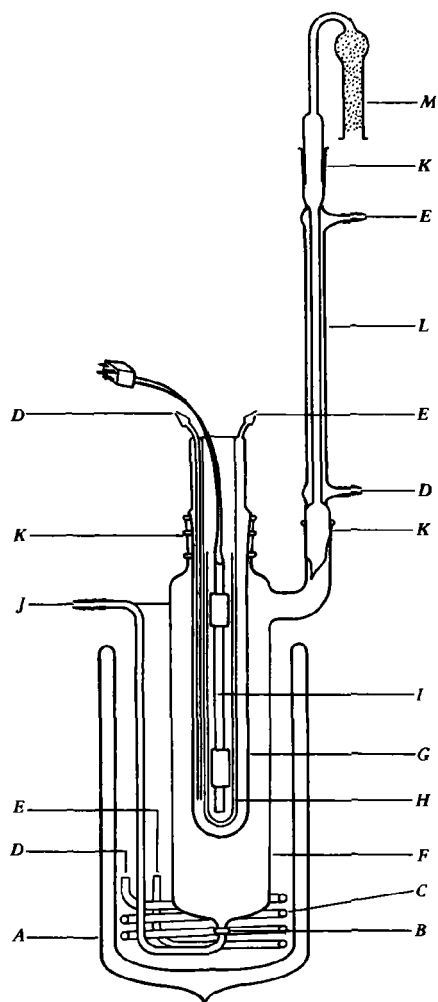


Figure 1. *A*, Dewar flask; *B*, sintered glass filter; *C*, metal cooling coil; *D*, water inlet; *E*, water outlet; *F*, reaction vessel; *G*, quartz immersion well; *H*, pyrex filter; *I*, lamp; *J*, nitrogen gas inlet; *K*, ground glass joint; *L*, condenser; *M*, calcium chloride drying tube.

The preceding crude photo-adduct without purification is dissolved in 250 ml. of methanol and transferred to a 1-l., three-necked, round-bottomed flask fitted with overhead stirrer with Teflon blade, addition funnel, and argon inlet. The solution is cooled with an ice bath and 500 ml. of 4 *M* aqueous sodium hydroxide is added over a period of 20 minutes with stirring. Upon completion of the addition, the ice bath is removed and stirring is continued for 16 hours. The brown solution is then extracted with four 500-ml. portions of chloroform. The organic extract is washed with saturated sodium chloride solution, dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Distillation of the residue through a 6-cm. Vigreux column affords, after a small forerun, 23.0–27.9 g. (47–57%) of 7-hydroxy-4,4,6,7-tetramethylbicyclo[4.2.0]octan-2-one (Note 8) collected at 92–101° (0.2 mm.).

A 2-l., three-necked, round-bottomed flask, fitted with an overhead stirrer with Teflon blade, a Fries condenser, and a stopper, is charged with a solution of 9.8 g. (0.05 mole) of 7-hydroxy-4,4,6,7-tetramethylbicyclo[4.2.0]octan-2-one in 600 ml. of 50% (by volume) aqueous acetonitrile and 82 g. (0.15 mole) (Note 9) of ceric ammonium nitrate (Note 10) is added in one portion with stirring. Immediately after completion of the addition, the flask is immersed in an oil bath preheated to 170°. Refluxing occurs in about 10 minutes and is continued for 5 minutes. During this period the color of the solution changes from light brown to pale yellow. At the end of this time the reaction mixture is immediately poured onto crushed ice and extracted with four 600-ml. portions of chloroform. The combined extracts are washed with saturated sodium hydrogen carbonate and then saturated sodium chloride, dried over magnesium sulfate, and filtered. The solvent is removed under reduced pressure and the residue distilled, using a short-path distillation apparatus. All material boiling at 70–100° (0.25 mm.) is collected. Fractionation of the yellow oil through a 6-cm. Vigreux column gives 4.68–4.71 g. (48–50%) of 3,5,5-trimethyl-2-(2-oxopropyl)-2-cyclohexene-1-one, b.p. 81–85° (0.4 mm.) (Note 11).

2. Notes

1. Isophorone obtained from M C and B Manufacturing Chemists was freshly distilled, b.p. 73° (4.5 mm.).
2. In order to minimize the formation of cyclohexenone dimer and to

achieve cleaner photo-adduct, it is essential to use a large excess of olefin in the photocycloaddition of a cyclohexenone to an olefin.³

3. Supplied by Aldrich Chemical Company, Inc.

4. Submitters used nitrogen purified by passing it through a set of gas wash bottles containing Fieser's solution,⁴ concentrated sulfuric acid, sodium hydroxide, and calcium chloride.

5. The submitters filled the Dewar flask with ice and water. After 2 hours the ice had melted and water was left in the flask for cooling.

6. The progress of the reaction was monitored by injecting after each 24-hour period an aliquot into a gas chromatograph and checking the peak corresponding to isophorone. Alternatively, thin-layer chromatography (E. Merck 0.25-mm. silica gel plates developed with ethyl acetate) can be used.

7. This crude product is contaminated mainly by polymeric compounds. An attempted distillation of this material was unsuccessful; partial decomposition occurred at 110–125° (0.3 mm.). If it is desirable, purification can be achieved by extensive silica gel column chromatography with 5% ether in benzene.

8. The product is a mixture of at least two diastereomers as indicated by its proton magnetic resonance spectrum (carbon tetrachloride) showing eight singlets at δ 0.9–1.22 for a total of twelve methyl protons. Its ir spectrum (neat) exhibits absorption bands at 3440 and 1695 cm^{-1} . A molecular ion peak at 196.1447 (calcd. for $\text{C}_{12}\text{H}_{20}\text{O}_2$:196.1463) is displayed in its mass spectrum.

9. Use of less of the reagent resulted in partial recovery of the starting material.

10. Procured from Fisher Scientific Company.

11. Infrared (neat) cm^{-1} : 1720, 1670, 1645; proton magnetic resonance (chloroform-*d*) δ : 1.03, 1.87, 2.13, 2.20, 2.25, 3.43 (all singlets); mass spectrum m/e 194.1299 (M^+).

3. Discussion

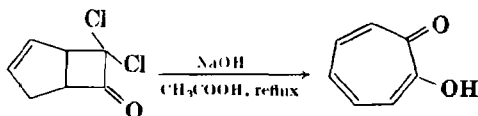
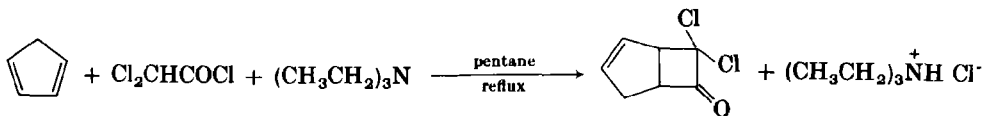
In recent years the application of photocycloaddition reactions to organic synthesis has been growing in importance.^{5,6} The procedure described is illustrative of a general method³ based on a photocycloaddition reaction for the introduction of an activated alkyl group specifically to the α -carbon atom of an α,β -unsaturated cyclohexenone. Especially significant is the fact that the method is also applicable to

α,β -unsaturated cyclohexenones which do not possess any enolizable γ -hydrogen atom and thus to which normal alkylation reactions⁷ cannot be applied. A closely related procedure involving the photocycloaddition of vinyl acetate to 2-cyclohexenones (in which enolization toward the 6-position is forbidden) followed by bromination and fragmentation of the adduct has been reported.^{3,8} It has also been observed⁹ that photo-adducts of cycloalkenones and vinylene carbonate undergo fragmentation upon alkali treatment giving 2-(2-oxoethyl)-2-cycloalken-1-ones.

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TROPOLONE

[2,4,6-Cycloheptatrien-1-one, 2-hydroxy-]



Submitted by RICHARD A. MINNS¹

Checked by ARTHUR J. ELLIOTT
and WILLIAM A. SHEPPARD

1. Procedure

A. *7,7-Dichlorobicyclo[3.2.0]hept-2-en-6-one*. In a 2-l., three-necked, round-bottomed flask fitted with an addition funnel, a reflux condenser, and a mechanical stirrer are placed 100 g. (0.68 mole) of dichloroacetyl chloride (Note 1), 170 ml. of cyclopentadiene (2 moles) (Note 2), and 700 ml. of pentane (Note 3). The solution is heated to reflux under nitrogen and rapidly stirred while a solution of 70.8 g. (0.70 mole) of triethylamine (Note 4) in 300 ml. of pentane is added over a period of 4 hours (Note 5). After the cream-colored mixture has been refluxed for an additional 2 hours, 250 ml. of distilled water is added to dissolve the triethylamine hydrochloride; the layers are separated in a 2-l. separatory funnel. After extraction of the aqueous layer with two 100-ml. portions of pentane, the combined organic layers are filtered and dried by passage through absorbent cotton. Pentane and excess cyclopentadiene are then removed by rapid distillation. The resulting viscous, orange liquid is fractionally distilled under reduced pressure through a 30-cm. Vigreux column. Heat is supplied from an oil bath held at 105°. During collection of the first fraction, which consists mainly of dicyclopentadiene (Note 6), b.p. 61–62° (9 mm.), the cold finger and take-off tube must be warmed periodically with a heat gun to prevent plugging. The 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one, 101–102 g. (84–85%), is collected as a colorless liquid, b.p. 66–68° (2 mm.), n_D^{25} 1.5129, having a purity > 99% as determined by gas chromatographic analysis (Notes 6, 7).

B. *Tropolone*. In a 1-l., three-necked, round-bottomed flask equipped with a mechanical stirrer, addition funnel, and reflux condenser are placed 500 ml. of glacial acetic acid and then, *cautiously*, 100 g. of sodium hydroxide pellets. After the pellets have dissolved, 100 g. of 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one is added and the solution is maintained at reflux under nitrogen for 8 hours. Concentrated hydrochloric acid is then added until the mixture is about pH 1; approximately 125 ml. of acid is required. After the addition of 1 l. of benzene, the mixture is filtered and the solid sodium chloride is washed with three 100-ml. portions of benzene. The two phases of the filtrate are separated and the aqueous phase is transferred to a 1-l. continuous extractor (Note 8) which is stirred magnetically. The combined benzene phase is transferred to a 2-l. pot connected to the extractor and the aqueous phase is extracted for 13 hours. Following distillation of the benzene, the remaining orange liquid is distilled under reduced pressure

through a 30-cm. Vigreux column to remove acetic acid. When tropolone begins to distill into the column, the condenser is replaced by a two-necked flask immersed in ice water. With vacuum applied through one neck of this receiver, tropolone distills at 60° (0.1 mm.) and is collected as a crude yellow solid, 66.4 g. (96%). A solution of the impure product in 150 ml. of dichloromethane is diluted with 600 ml. of pentane, 4 g. of activated carbon is added, and the mixture is heated to boiling. After removal of the carbon by filtration, the solution is maintained at -20° until crystallization is complete. Tropolone, 53 g. (77%) (Note 9) as white needles, m.p. $50-51^{\circ}$, is collected by filtration. Evaporation of the filtrate to dryness, dissolution of the residue in 800 ml. of pentane, treatment with activated carbon, and cooling to -20° yields an additional 8 g. (12%) of tropolone as pale-yellow crystals, m.p. $49.5-51^{\circ}$.

2. Notes

1. Freshly opened bottles of dichloroacetyl chloride from Aldrich Chemical Company, Inc., were used. The acid chloride can also be prepared by the dropwise addition of 1 volume of dichloroacetic acid to 2.5 volumes of phthaloyl chloride heated to 140° . After the addition is complete, the solution is vigorously heated and dichloroacetyl chloride, b.p. $106-108^{\circ}$, is distilled through a 30-cm. column packed with glass beads; the yield is 85%.

2. Cyclopentadiene was prepared by cracking dicyclopentadiene² of 95% purity purchased from Aldrich Chemical Company, Inc.

3. Technical grade pentane from Fisher Scientific Company was used.

4. Triethylamine from Eastman Organic Chemicals was used without further purification.

5. Faster addition results in some polymerization of the dichloro-ketene which darkens the precipitate.

6. Fractions were analyzed by vapor-phase chromatography (column: 0.3×120 cm., 20% SE-52 on Chromosorb P 60/80, 130° , helium flow rate of 60 ml./min.). Retention times of 1.9 minutes for dicyclopentadiene and 4.6 minutes for the 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one were found.

7. The 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one has the following spectral characteristics: infrared (neat) cm.^{-1} : 1806 ($\text{C}=\text{O}$), 1608 ($\text{C}=\text{C}$); proton magnetic resonance (carbon tetrachloride) δ (multiplicity, num-

ber of protons, assignment): 2.70 (multiplet, 2, CH_2), 4.10 (multiplet, 2, bridgehead hydrogens), 5.90 (multiplet, 2, $\text{CH}=\text{CH}$).

8. A continuous extractor has been described earlier in this series.³

9. Tropolone has the following spectral characteristics: infrared (KBr pellet) cm^{-1} : 3210 (OH), 1613 ($\text{C}=\text{O}$), 1548 ($\text{C}=\text{C}$); proton magnetic resonance (chloroform- d) δ (multiplicity, number of protons, assignment): 7.33 (multiplet, 5, ring), 8.76 (singlet, 1, OH).

3. Discussion

Tropolone has been made from 1,2-cycloheptanedione by bromination and reduction,⁴ and by reaction with *N*-bromosuccinimide;⁵ from cycloheptanone by bromination, hydrolysis, and reduction;⁶ from diethyl pimelate by acyloin condensation and bromination;⁷ from cycloheptatriene by permanganate oxidation;⁸ from 3,5-dihydroxybenzoic acid by a multistep synthesis;⁹ from 2,3-dimethoxybenzoic acid by a multistep synthesis;¹⁰ from tropone by chlorination and hydrolysis,¹¹ by amination with hydrazine and hydrolysis,¹² or by photooxidation followed by reduction with thiourea;¹³ from cyclopentadiene and tetrafluoroethylene;¹⁴ and from cyclopentadiene and dichloroketene.^{15,16}

The present procedure, based on the last method, is relatively simple and uses inexpensive starting materials. Step A exemplifies the 2 + 2 cycloaddition of dichloroketene to an olefin,¹⁷⁻¹⁹ and the specific cycloadduct obtained has proved to be a useful intermediate in other syntheses.²⁰⁻²² Step B has been the subject of several mechanistic studies,²³⁻²⁶ and its yield has been greatly improved by the isolation technique described above. This synthesis has also been extended to the preparation of various tropolone derivatives.^{16,23,24,27-30}

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***tert*-BUTYL AZIDOFORMATE¹**

WARNING

Tests conducted by the Eastman Kodak Company have shown that *tert*-butyl azidoformate [Formic acid, azido, *tert*-butyl ester], also known as *tert*-butoxy carbonyl azide and *t*-BOC azide, is a thermally unstable, shock-sensitive compound (TNT equivalence: 45%).

A number of less-hazardous reagents that can be substituted for *tert*-butyl azidoformate in *tert*-butoxycarbonylation reactions are available including 2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile (Aldrich Chemical Company), *O*-*tert*-butyl *S*-phenyl thiocarbonate (Eastman Organic Chemicals), di-*tert*-butyl dicarbonate² and *tert*-butyl phenyl carbonate.³

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NOMENCLATURE

Both common and systematic names of compounds are used throughout this volume, depending on which the Editor-in-Chief feels is most appropriate. Preparations appear in the alphabetical order of names of the compound or names of the synthetic procedures. The *Chemical Abstracts* indexing name for each title compound, if it differs from the title name, is given as a subtitle. Because of the major shift to new systematic nomenclature adopted by *Chemical Abstracts* in 1972, many common names used in the text are immediately followed by the bracketed, new names. Whenever two names are concurrently in use, the correct *Chemical Abstracts* name is adopted. The prefix *n*- is deleted from *n*-alkanes and *n*-alkyls. All reported dimensions are now expressed in *Système International* units.

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data. In the event that any of the reactants are not commercially available at reasonable cost, their preparation should be described in as complete detail and in the same manner as the preparation of the product of major interest. The sources of the reactants should be described in notes, and physical properties such as boiling point, index of refraction, and melting point of the reactants should be included except where standard commercial grades are specified.

Beginning with Volume 49, Methods of Preparation (Sec. 3) and Merits of the Preparation (Sec. 4) have been combined into Discussion (Sec. 3). In this section should be described other practical methods for accomplishing the purpose of the procedure that have appeared in the literature. It is unnecessary to mention methods that have been published but are of no practical synthetic value. Those features of the procedure that recommend it for publication in *Organic Syntheses* should be cited (synthetic method of considerable scope, specific compound of interest not likely to be made available commercially, method that gives better yield or is less laborious than other methods, etc.). If possible, a brief discussion of the scope and limitations of the procedure as applied to other examples, as well as a comparison of the particular method with the other methods cited, should be included. If necessary to the understanding or use of the method for related syntheses, a brief discussion of the mechanism may be placed in this section. The present emphasis of *Organic Syntheses* is on model procedures rather than on specific compounds (although the latter are still welcomed), and the Discussion should be written to help the reader decide whether and how to use the procedure in his own research. Three copies of each procedure should be submitted to the Secretary of the Editorial Board. It is sometimes helpful to the Board if there is an accompanying letter setting forth the features of the preparations that are of interest.

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PREFACE

Through prudent selection, careful checking, and publication of procedures, *Organic Syntheses* has, since 1921, provided organic chemists with reliable experimental directions. The procedures appearing in these annual volumes provide specific examples of important synthetic methods or precise directions for the preparation of intriguing compounds, starting materials, or reagents. This volume contains 30 checked procedures.

Small rings, which continue to play key roles in synthetic and physical organic chemistry, are represented by seven procedures. A modern variation on a classic is provided by ACYLOIN CONDENSATION IN WHICH CHLOROTRIMETHYLSILANE IS USED AS A TRAPPING AGENT: 1,2-BIS(TRIMETHYLSILYLOXY)CYCLOBUTENE AND 2-HYDROXYCYCLOBUTANONE. Cyclobutanone makes its third appearance in the series, this time in CYCLOBUTANONE FROM METHYLENECYCLOPROPANE VIA OXASPIROPENTANE. Four-membered carbocycles are made by [2 + 2] cycloadditions and then ring-opened in 3,5,5-TRIMETHYL-2-(2-OXOPROPYL)-2-CYCLOHEXEN-1-ONE and TROPOLONE. 1,2-DIMETHYLCYCLOBUTENES BY REDUCTIVE RING-CONTRACTION OF SULFOLANES: *cis*-7,8-DIMETHYLBICYCLO[4.2.0]-OCT-7-ENE illustrates a widely applicable scheme in which the key step is similar to the Ramberg-Bäcklund reaction. The small ring category is rounded out by inclusion of CYCLOPROPENONE and a heterocycle 3-PHENYL-2*H*-AZIRINE-2-CARBOXALDEHYDE.

Synthetic applications of organosulfur reagents are expanding rapidly. Stable sulfuranes are included for the first time in BIS[2,2,2-TRIFLUORO-1-PHENYL-1-(TRIFLUOROMETHYL)ETHOXY]DIPHENYL SULFURANE and DIETHYLAMINOSULFUR TRIFLUORIDE. The latter is used to transform an alcohol to a fluoride in *p*-NITROBENZYL FLUORIDE. The direct homologation of a ketone to a nitrile by use of *p*-TOLYLSULFONYLMETHYL ISOCYANIDE is illustrated in 2-ADAMANTANECARBONITRILE. Reagents with

versatile reactivity profiles are provided in the preparations SULFONYL CYANIDES: METHANESULFONYL CYANIDE and *p*-TOLYL-SULFONYLDIAZOMETHANE.

The template effects of potassium and lithium ions are responsible for the efficiency of the synthesis of macrocyclic ligands in 18-CROWN-6 and 2,2,7,7,12,12,17,17-OCTAMETHYL-21,22,23,24-TETRAOXAPER-HYDROQUATERENE.

Concern for the conservation of energy and materials maintains high interest in catalytic and electrochemistry. Oxygen in the presence of metal catalysts is used in CUPROUS ION-CATALYZED OXIDATIVE CLEAVAGE OF AROMATIC *o*-DIAMINES BY OXYGEN: (*Z,Z*)-2,4-HEXADIENEDINITRILE and OXIDATION WITH BIS(SALICYLIDENE)ETHYLENEDIIMINOCOBALT(II) (SALCOMINE): 2,6-DI-*tert*-BUTYL-*p*-BENZOQUINONE. Hydroformylation of olefins, an important industrial method, is accomplished in a convenient lab-scale process in ALDEHYDES FROM OLEFINS: CYCLOHEXANE-CARBOXALDEHYDE. An effective and useful electrochemical synthesis is illustrated in the procedure 3,3,6,6-TETRAMETHOXY-1,4-CYCLOHEXADIENE.

Organotellurium intermediates and dienyl iron complexes make their debut in this volume. Raney nickel is used to transform a biaryltellurium dichloride to a biaryl in BIARYLS FROM SIMPLE ARENES VIA ORGANOTELLURIUM INTERMEDIATES: 4,4'-DIMETHOXY-1,1'-BIPHENYL. The preparation of dienyl iron complexes which undergo hydride abstraction with triphenylmethyl tetrafluoroborate is illustrated in TRICARBONYL [(2,3,4,5- η)-2,4-CYCLOHEXADIEN-1-ONE]IRON AND TRICARBONYL[(1,2,3,4,5- η)-2-METHOXY-2,4-CYCLOHEXADIEN-1-YL]IRON(1+) HEXAFLUOROPHOSPHATE FROM ANISOLE. The dienone complex is an effective phenylating agent for aromatic amines; the dienyl salt reacts with many nucleophiles exemplified by ALKYLATION OF DIMEDONE WITH A TRICARBONYL(DIENE) IRON COMPLEX: TRICARBONYL-[2-[(2,3,4,5- η)-4-METHOXY-2,4-CYCLOHEXADIEN-1-YL]-5,5-DIMETHYL-1,3-CYCLOHEXANEDIONE]IRON.

Reactions of carbon nucleophiles with organohalogen compounds have great diversity for the construction of new carbon-carbon bonds. The intriguing synthon, ethoxyethynylsodium, is generated and alkylated in 1-ETHOXY-1-BUTANE. Following an alkylation of propynylsodium, a vinyl halide is generated in a stereoselective manner

involving a curious halogen migration in (Z)-4-CHLORO-4-HEXENYL TRIFLUOROACETATE. A problem of constant interest, control of enolate alkylation, is dealt with in MONOALKYLATION OF α,β -UNSATURATED KETONES VIA METALLOENAMINES: 1-BUTYL-10-METHYL- $\Delta^{1(9)}$ -2-OCTALONE. Alkylation of methyl nitroacetate with methyl bromoacetate affords the versatile starting material DIMETHYL NITROSUCCINATE. Nucleophilic displacement of fluoride from hexafluorobenzene proceeds readily in a slick synthesis of (PENTAFLUOROPHENYL)ACETONITRILE.

The functionalized allene, DIMETHYL 2,3-PENTADIENEDIOATE, the first in the series, is an intriguing substrate for various addition and cycloaddition reactions. Finally, a new reagent, DI-*tert*-BUTYL DICARBONATE, for the formation of *N*-*t*-BOC derivatives which eliminates the use of the hazardous *tert*-BUTYL AZIDOFORMATE (WARNING) is introduced.

The Board of Editors welcomes both the submission of preparations for future volumes and suggestions for change that will enhance the usefulness of *Organic Syntheses*. Submitters are kindly asked to examine the instructions on pages v and vi that describe the type of preparation we wish to receive and also the information to be included in each contribution. A style guide for preparing manuscripts is available from the Secretary to the Board, and submitters are requested to follow its instructions.

As in previous volumes of *Organic Syntheses* unchecked procedures are tabulated at the end of this volume. Of the preparations received between May 16, 1976, and June 30, 1977, only those that have been accepted by the Board of Editors for checking are listed. These unchecked procedures are available from the Secretary's office for a nominal fee.

The Editor-in-Chief wishes to acknowledge a number of people for their efforts on behalf of *Organic Syntheses*. First I would like to acknowledge the submitters who have generously agreed to openly share their experimental expertise in the precise manner required by *Organic Syntheses* and who have patiently borne with us during the checking and editing process. My colleagues on the Board of Editors and their collaborators have checked many of the procedures included in this volume. I would like to take this opportunity to warmly thank my own coworkers for sharing with me a belief in the importance of this work and contributing their laboratory efforts to this and other volumes of

Organic Syntheses. Special credit must go to Professor Wayland Noland, Secretary to the Board, for skillfully organizing the sea of paper from which this volume finally floated. Thanks are due to Miss Amy Harrison, Miss Carol Schaap and Miss Elly Sparwirt for typing the manuscript. Dr. Susan Goff assisted with the preparation of the indexes.

CARL R. JOHNSON

Dearborn, Michigan
July 1977

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